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JOURNAL
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AMERICAN PHARMACEUTICAL ASSOCIATION

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THE SEVENTY-FIRST ANNUAL CONVENTION OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN ASHEVILLE, N. C.

The 1923 meetings of the American Conference of Pharmaceutical Faculties and the National Association of Boards of Pharmacy will also be held in Asheville.

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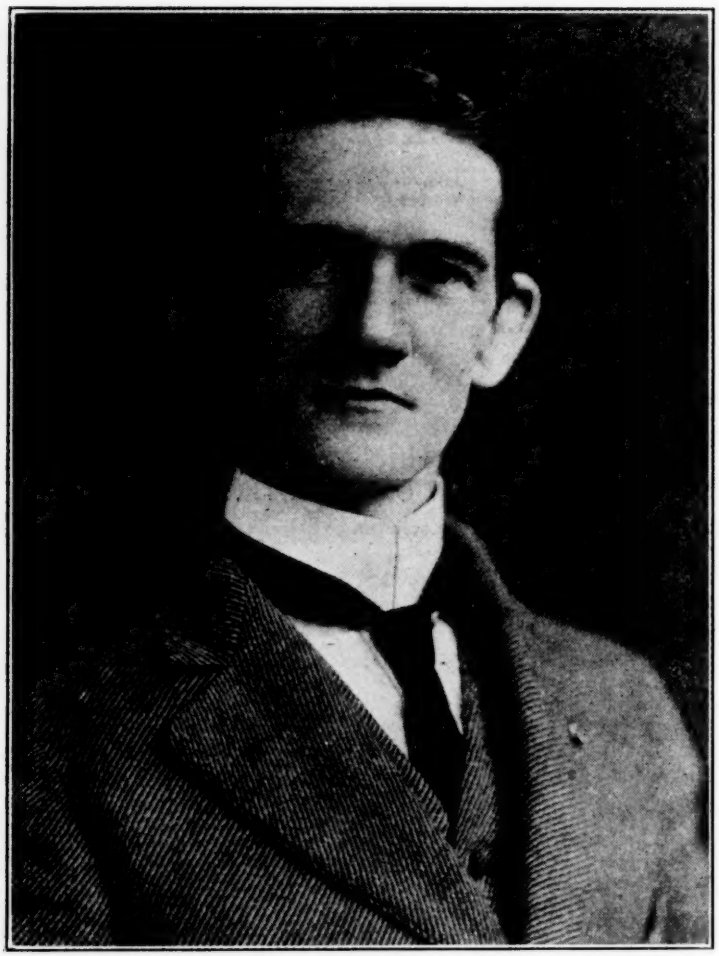
EDWARD HENRY WALSDORF

NEW ORLEANS, LA.

President of the National Association of Boards of Pharmacy, 1922-1923



EDWARD H. WALSDORF

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XI NOVEMBER, 1922 No. 11

EDWARD HENRY WALSDORF.

Appreciative of the election of Mr. Walsdorf as President of the National Association of Boards of Pharmacy, our fellow-member, Editor Christian Schertz, wrote a biographic editorial relating to the former for *The Modern Druggist;* liberty is taken by quoting (not *verbatim* but in substance) at length therefrom in adapting the matter to this brief sketch:

"As President of the Louisiana State Board of Pharmacy, Mr. Walsdorf has the record of being appointed by four Governors; it seems fitting that a man so highly considered by his own state's chief executives should be elected president of a national association. His record is one that may be pointed out to the youth entering pharmacy as a worthy example to follow. It is very difficult to write of a man known personally and intimately by this publication (*The Modern Druggist*) without erring in good taste; we do not desire to be charged with effusiveness such as one is susceptible to in discussing a tried friend, yet it does not seem just to the young men who are about to enter colleges of pharmacy, or who are preparing to pass the state board examinations, to withhold from them knowledge of our consideration and appraisal that is a tribute to one of our fellows. Mr. Walsdorf is a 'self-made' man in every sense of the word. He has had no patron; owes no man a dollar for his start, and has climbed to the pinnacle through decent methods of industry and long hours under the lamp while others slept. It is not in every man's power to do what he has done, but we deny that there is any element of luck in his achievements. 'There is a destiny which shapes our ends,' and the subject of this sketch has made the obligation required by that destiny straight and true and has now gained the logical reward. We bespeak the congratulations of the drug fraternity as we know there is no envy; all of us have pride in the new honors that have come to him."

Mr. Walsdorf will be fifty years old on the 13th of next month. He is a native of the Crescent City and was educated in McDonough Schools. He entered business in 1895, and at one time was the owner of seven drug stores in New Orleans but in later years he has concentrated his energies in two.

He was president of Louisiana State Pharmaceutical Association in 1913, and rendered valuable service before and since on important committees. In 1909,

he was appointed member of Louisiana Board of Pharmacy by Governor Jared Y. Sanders and successively by Governors Hall, Pleasant, and Parker; his term of office expires in 1925. For a number of years he was secretary of the Board and is now the president.

When the National Association of Retail Druggists met in New Orleans (1921), Mr. Walsdorf was chosen local secretary; he served as chairman of the Registration Committee during the convention of the American Pharmaceutical Association, and as chairman of other local committees. The esteem in which he is held was evidenced by a banquet given in his honor soon after his return from the Cleveland A. Ph. A. meeting, which was largely attended by other business and professional men, besides pharmacists. He is president of the Ewing Market Business Men's Association. The president of the N. A. B. P. is professor of "Commercial Pharmacy" in Tulane University College of Pharmacy.

Mr. Walsdorf married Delia T. Stewart of Mobile, Ala., in 1896; they have one daughter, Thelma Warrene, and two sons, Edward Henry and Harold Norman. Mrs. Walsdorf took an active part in the entertainments for A. Ph. A. members at New Orleans, and attended the Cleveland Convention. In city and state affairs both Mr. and Mrs. Walsdorf enter with the same enthusiasm that marks the former's activities in matters pharmaceutical.

E. G. E.

NEW PROGRAM OF VETERANS' BUREAU.

Director Charles R. Forbes has announced that a material improvement in the medical service and treatment of disabled ex-service men will occur as a result of the new program undertaken by the U. S. Veterans' Bureau. Construction of new hospitals under the second Langley bill, he reports, will give the bureau a sufficient number of beds, under direct government management and supervised by government medical officers, to assure proper care of all soldier-patients. The list of hospitals projected by the bureau includes:

A neuropsychiatric hospital at Northampton, Mass., the groundwork and foundation of which are now being constructed.

A 500-bed neuropsychiatric hospital at Chillicothe, Ohio, the bids for which have recently been received.

A 500-bed tuberculosis hospital at Chelsea, N. Y., to be constructed jointly by the Treasury Department and the U. S. Veterans' Bureau.

The Methodist Hospital at Memphis, Tenn., recently purchased to be used for general medical and surgical cases.

A neuropsychiatric hospital at Camp Lewis, Wash., plans and specifications to be ready before October 15.

A hospital for mental cases at Knoxville, Iowa, now being designed and planned.

A project at Livermore, Calif., for which bids will be ready within the near future.

A tuberculosis hospital at Tupper Lake, N. Y., for which ground excavations have been started.

A hospital at Gulfport, Miss.

A neuropsychiatric hospital, to be erected at Camp Custer, Mich.

A hospital to be constructed at St. Cloud, Minn.

Director Forbes declared that, with these hospitals completed, disabled war veterans will be promptly transferred from all contract hospitals in the country.

EDITORIAL

E. G. EBERLE, Editor 253 Bourse Bldg., PHILADELPHIA

PROTECTING SCIENTIFIC RESEARCH.

LEGISLATION that will interfere with scientific medical and pharmaceutical research should incite coöperative counter-efforts on the part of doctors and pharmacists. Legislation of the kind referred to is contemplated, and, in some states, favorable action was sought at the polls.

Reason indicates that the "Death Bill" in Colorado will not be endorsed by the people, but further efforts will be made in behalf of legislation of this kind—therefore this comment. The selfish motive almost invariably enters into the promotion of this type of legislation; usually, the intentions are more far-reaching than is gleaned from a casual reading of proposed measures, and evidenced by the proponents. No attempt is made at this time to discuss such motives by any interests, but only to direct attention to some of the results that might or would follow the passage of a bill like that voted on in Colorado. This bill if enacted into law would make punishable by fine and imprisonment "any painful experiment, operation or administration upon an animal without the use of anesthetics." The *Rocky Mountain Druggist* comments that "the bill is sweeping in its scope and would not only prevent the use of laboratory animals by agriculturalists, veterinarians, and physicians, but, if strictly interpreted, would make it illegal to exterminate vermin, to hunt and fish, and even to kill animals for food."

There can hardly be any question relative to the contemplated prohibition by the measure of the use of test animals in standardizing drugs and determining their strength and efficiency, and such intent in legislation should be sufficient incentive to call forth the opposition of pharmacists. E. G. E.

SCIENTIFIC RESEARCH DETERMINES FACTS.

SCIENTIFIC research is being applied in all activities, because it determines facts and does away with guesswork; that empirical experiments contributed largely to the progress of science no one will deny—Sir Humphrey Davy discovered the principle that has made possible the establishment of the electrochemical industry; electric welding resulted from experiments of another character; the listening through the ground, on dark nights, to determine the direction in which cattle were straying, has made possible the long-distance transmission of telephonic and telegraphic messages; Faraday's experiments with gases gave us the benefits of anesthesia; the discovery of the way to separate nickel from copper resulted from study in the fight to control a yellow-fever epidemic. References of one type or another could be multiplied, but the point in research is to determine; while the results may not always be those expected, guesswork is deprived of some of its secrets thereby.

In the modern cultivation of medicinal plants the purpose is not so much to increase acreage as to make the plants larger producers of active constituents, in one way or another. As Floyd W. Parsons rightly says: "In an era of national scientific research the farmer will not seek to supply the increased demand for a product of the soil by simply adding additional acreage, but will discover a way to get more of the product from each acre cultivated. So in the factory, the management will not serenely assume that a larger output entails more men, but rather that the solution involves an increased production per individual." These are results of scientific research in the industries.

A report in a bulletin on research of the Chamber of Commerce of the United States says that American industry is spending about $70,000,000 annually on scientific research. The bulletin states that about one-half of this sum is spent by American manufacturers in the conduct of laboratory research, while the remainder is expended in experimental and development work plants. The further statement is made that, as a result of scientific research work, approximately one-half billion dollars are saved annually by industry in this country.

"The value of scientific research, both from an economic and industrial standpoint," the department bulletin says, "has never been so fully appreciated as at the present time. The problems of the recent war forced science and its research activities to the front in all civilized countries. It is now realized by leading manufacturers that scientific investigation is a necessary adjunct to efficient coöperation. A utilization of the scientific knowledge now available, and a sympathetic coöperation in the free interchange of such information will lead to the adoption of improved manufacturing processes and do much to obviate the danger of ignorant destructive competition. The realization of this fact is shown by the 500 or more firms now maintaining laboratories for industrial research."

There is an interdependence of the professions and the industries—in practice, in trade and commerce, and an interrelation in scientific investigation. E. G. E.

DANGERS PRESENTED BY THE FREE SALE OF LIVING PATHOGENIC CULTURES.

FROM THE FRENCH—BY WM. H. GANO.

An interesting article has recently been published in *Annales d'hygeine publique et de medicine legale*, pointing out the dangers of the unrestricted sale of living pathogenic germs, which could be used for criminal ends.

The affair of one Girard directed the attention of the writer toward the matter.

This Girard was accused of having poisoned several persons, upon whose lives he had effected insurance in his own favor.

Girard did not expiate the crime for which he was convicted—because he died before the courts passed sentence upon him—but the information obtained against him showed the method he used in order to realize his diabolical designs.

When he was mobilized, Girard had already an experience with the police—he was surprised in the very act of robbery. A search of his domicile disclosed tubes of microbic cultures, ampuls of strychnine sulphate and of potassium cyanide, some cocaine, a number of pharmaceutical preparations, a microscope, and a work on toxicology. Questioned by the military judge, Girard replied

that he devoted himself, for amusement, to the microscopic examination of microbes. An order of "not sufficient evidence" intervened—an expert having testified that this individual presented numerous psychological defects.

Emboldened by this immunity Girard felt encouraged in his criminal projects, and continued to interest himself in microbic cultures which seemed to him capable of causing death, without leaving traces, as mineral or vegetable poisons will do. He purchased works on medical law, a book on typhoid fever, a high-power microscope, an oven, and all the necessary material and apparatus for growing bacteria. It was found that he had purchased cultures of anthrax and other bacilli from two firms in Paris, and that he renewed these supplies periodically.

At a given time, M. Delmas and five other persons, M. and Mme. Pernotte and their three sons, were stricken with typhoid fever. But these six persons recovered. The five members of the Pernotte family were stricken simultaneously with typhoid symptoms—it was evident that their contamination was due to one and the same cause.

It was established that Girard frequented the Pernotte home; that he went there in the morning and that he always waited in the dining-room; that the servants ate the same food as the master, but that they did not drink the same water—the Pernotte family drinking the water from a "water cooler." As the domestics remained immune it was properly surmised that the trouble came through the drinking water, and it was believed that Girard poured cultures of the typhoid bacillus into the "water cooler" during his visits; this hypothesis became more probable when it was learned that one of the supply houses had, about this date, made several deliveries of typhoid bacilli to Girard. The judge expressed astonishment that persons foreign to the medical sciences could so easily procure these dangerous agents.

Upon request of the court it was shown that after adding 1 cc of typhoid culture to 1 liter of filtered drinking water, 25% of the bacilli were living after standing 7 days; in beer, 8% were living at the end of 24 hours; the acidity caused the germs to disappear in less than 24 hours, when placed in wine or cider. The Girard affair is not the only one showing the need of strict regulation in this matter—a case has occurred in Germany analogous to that of Girard: One Hopf procured from a well-known firm in Vienna some thirty different pathogenic microbic cultures, among others—cultures of typhoid, anthrax, cholera, plague, botulism, tetanus, all with criminal intent; he confessed to having administered to his *third wife* typhoid bacilli in chopped meat.

Since 1904 regulations concerning the circulation and manipulation of these germs have been vigorously enforced in Germany, but the Hopf case has provoked new and more severe supervision.

There has been a bill proposed in the French Chamber of Deputies to strictly regulate the delivery of cultures of living pathogenic germs, and to confine such delivery to persons who are scientifically qualified to care for and handle the same.

A CONTRIBUTION TO THE CHEMICAL–PHARMACODYNAMIC RELATIONSHIPS OF ATROPINE AND HOMATROPINE.*

BY DAVID I. MACHT.†

INTRODUCTION.

The structure of the atropine molecule and the relation of its chemical structure to the pharmacological effects of the alkaloid are perhaps better known than those of most other pharmacological agents. While the medicinal use of various members of the Belladonna family goes back to remote antiquity the discovery of their active principles is of a comparatively recent date. Atropine was discovered in 1831 by Mein who isolated it from the root of *Datura*.[1] The same substance in pure form was independently and almost simultaneously obtained by Geiger and Hesse.[2] These latter investigators gave some of their base to Liebig for analysis and Liebig gave the empirical constitution of the substance $C_{17}H_{23}NO_3$.[3] This formula was confirmed by Planta[4] and is the accepted empirical formula for atropine at the present day. The chemical structure of this alkaloid has been elucidated beginning with the interesting observations of Kraut[5] and Lossen[6] and by eminent chemists after them. Kraut and Lossen found that atropine on hydrolysis with hydrochloric acid or sodium hydroxide is broken into a base, called tropine, and an acid, named tropic acid; while on hydrolyzing with baryta water the decomposition products are tropine and atropic acid which differs from tropic acid by one molecule of water. Following these observations the work on the chemical structure of tropine, tropic acid and related compounds was continued especially by Merling,[7] Wilstätter[8] and Ladenburg[9] until the present accurate conception of the atropine molecule was attained. The culmination of the various studies on the subject may be said to be the synthesis of atropine by Ladenburg in 1879.[9] This achievement is the first instance of an artificial synthesis of a natural alkaloid in the laboratory.

The pharmacological properties of atropine and its decomposition products have been investigated by a number of authors. Fraser[10] studied the properties of tropine and tropic acid as compared with atropine itself. He found that while atropine is a powerful mydriatic, tropine itself has very little effect on the pupil of the eye. The same results were obtained by Hellmann;[11] Buchheim also studied the pharmacological properties of tropine as compared with atropine and found that tropine itself is practically inert both as regards its effect on the eye and the vagus inhibition of the heart.

Following the chemical studies of Ladenburg who decomposed atropine into the base tropine and tropic acid and could synthesize atropine by combining tropine with tropic acid again, that author prepared a number of other combinations of tropine with various acid radicals to which he gave the collective name of *tropeines*. Thus one of his preparations was salicyl tropeine, another phthalyl tropeine and still another oxytoluyl tropeine. This last compound which is a combination of tropeine with mandelic acid he named *homatropine*. The properties of this new synthetic alkaloid were examined for him by the physiologists Völckers and Quinke[12]

* The expenses of this investigation have been supported in part by a grant from the Research Fund of the American Pharmaceutical Association.

† From the Pharmacological Laboratory, Johns Hopkins University.

who found it to be a very powerful mydriatic and superior to atropine in that the mydriasis was of a shorter duration. The drug very quickly came into widespread use by ophthalmologists and is to-day perhaps the most important mydriatic in clinical practice.

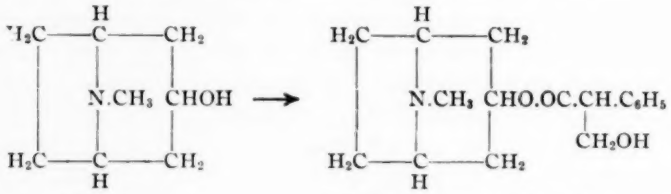
While the pharmacology of atropine is very well known the pharmacodynamics of homatropine have received very little attention. It is a matter of common knowledge that perhaps the most characteristic effect of atropine is its selective action on the myoneural junctions of the bulbo-sacral autonomic or parasympathetic nervous system, which junctions this alkaloid depresses or paralyzes. Thus the mydriasis produced by atropine is due to a paralysis of the myoneural junctions or endings of the oculomotor nerve; the inhibition of intestinal peristalsis produced by it is due to the depression of the vagus terminals in the intestinal walls; the loss of inhibition of the heart rate, produced by the same drug, is due to the paralysis of the vagus terminals in the heart, etc. Furthermore it is well known that this peculiar and selective action of atropine is due to the effect of the atropine molecule *as a whole*, that is, it is produced by the chemical combination of the base tropine with the tropic acid. Tropine alone or tropic acid alone does not exhibit these pharmacological properties. It has been generally assumed that homatropine, being a tropine and therefore closely related to a tropine chemically, produces its pharmacological effects in the same way as atropine; that it produces mydriasis through the paralysis of the oculomotorural nerve endings, etc. An examination of the literature on the pharmacology of homatropine, however, fails to bring evidence in support of this view. In the first place, very little experimental work on the pharmacology of homatropine has been done altogether. In the second place, what experimental evidence there is, points to properties possessed by homatropine which are quite different from those of atropine. Thus, for instance, de Schweinitz and Hare[13] noted that after the administration of homatropine the pulse instead of becoming more rapid is actually slowed and the same observation has been made by other authors. Even the few experiments made by Zulick[14] to clear up this point have not served to elucidate the pharmacodynamics of homatropine—indeed, have only served to complicate the subject.

The present author originally became interested in the pharmacological effects of homatropine through a study of mandelic acid. This acid is closely related and indeed is made from benzaldehyde and inasmuch as the author has already shown[15] that benzaldehyde exhibits the peculiar antispasmodic properties of benzyl alcohol and certain benzyl esters, it was thought that the mandelic radical in homatropine might play a rôle in its pharmacological action. Accordingly, an extensive study was begun of homatropine on the one hand and its decomposition products on the other. To analyze further the chemical and physiological relationships of homatropine, comparative studies of homatropine were made with those of atropine itself and a number of related derivatives. The effects of these were studied on the heart, eye, various smooth muscle viscera, etc., and are described hereafter.

CHEMICAL STRUCTURE.

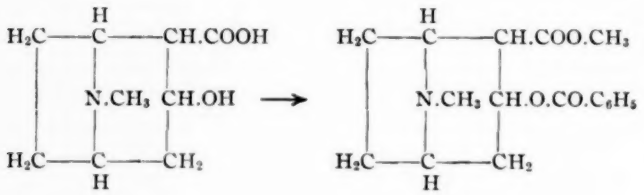
The chemical structure of atropine and homatropine is at present very completely established. The following formulas convey graphically the various chemical relationships. It will be seen that atropine consists of a combination of

tropine and tropic acid. Tropine itself may be regarded as the combination of pyrimidine and pyridine nuclei, that is, of a five-membered and six-membered aromatic ring with a nitrogen atom common to both. As is well known tropine is very closely related to the base ecgonine and the formulas in Fig. 2 reveal the close relationship between the important alkaloids, atropine and cocaine.



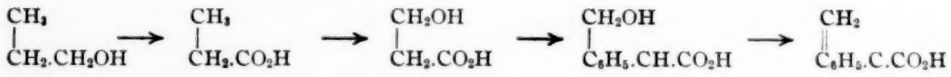
Tropine. Tropine tropate = Atropine.

Fig. 1.



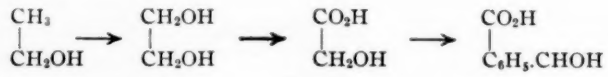
Ecgonine. Cocaine.

Fig. 2.



Propyl alcohol. Propionic acid. β-Hydroxy-propionic acid (hydracrylic acid). α-Phenyl-hydracrylic acid (tropic acid). α-Phenyl-acrylic acid (atropic acid).

Fig. 3.



Ethyl alcohol. Glycol. Glycolic acid (hydroxyacetic acid). Phenyl-glycolic acid (mandelic acid).

Fig. 4.

The structure of tropic acid is shown by Fig. 3. Starting with propyl alcohol we note the structure of propionic acid, of β-hydroxypropionic acid or hydracrylic acid and of tropic acid which is simply an α-phenylhydracrylic acid. Atropic acid is derived from tropic acid by abstraction of a molecule of water. Fig. 4 shows the structure of mandelic acid. Starting with ethyl alcohol we pass to glycol and from this to glycolic acid. Mandelic acid is phenylglycolic acid. It is important to bear the chemical structure of these compounds in mind in order to appreciate the pharmacological properties of the same as described above.

EFFECT OF ATROPINE AND HOMATROPINE ON THE VAGUS.

The effect of atropine on the heart is familiar to all. When a small dose of atropine sulphate is injected intravenously in a dog the myoneural junctions of the vagus in the heart are completely paralyzed so that stimulation of the vagus nerve electrically or otherwise fails to slow the heart action. Simultaneously with the paralysis of the vagus terminals and consequent loss of normal inhibitory impulses to the heart, the rate is accelerated and the blood pressure rises to a moderate degree. One milligram of atropine sulphate is generally sufficient to produce complete paralysis of the vagus terminal in the heart of a medium-sized dog as is well known to every student of physiology and pharmacology. If a similar experiment is performed with the use of homatropine, however, a different picture is obtained. The author has given numerous injections of homatropine to dogs and other animals and studied the effects of the same on the vagus and the heart. In the first place, after injecting a small dose (1 to 3 mg.) of homatropine it was noted that practically no effect on the vagus was produced at all as shown by electrical stimulation of the nerve. It requires from six to ten times as much homatropine as atropine to be injected before paralysis of the vagus terminals in the heart is produced so that the heart can no longer be inhibited by electrical

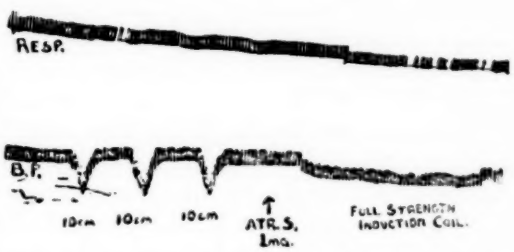


Fig. 5.—Dog 12 kilos, paraldehyde anesthesia. Effect of atropine, 1 mg., on electrical stimulation of the vagus. Upper curve respiration, lower curve blood pressure.

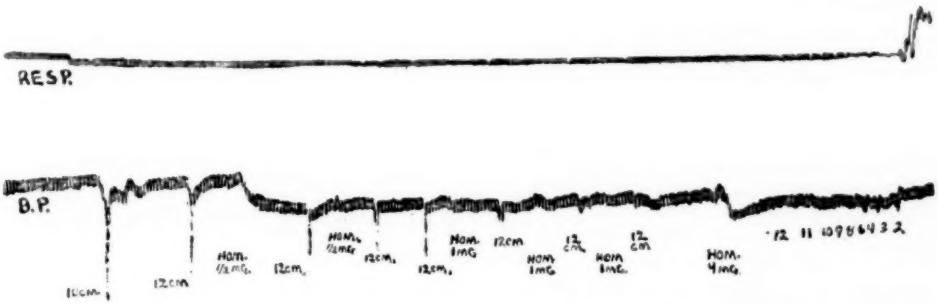


Fig. 6.—Dog 10 kilos, paraldehyde anesthesia. The effect of homatropine hydrochloride on electrical stimulation of vagus. Upper curve respiration, lower curve blood pressure.

stimulation of the vagus nerve trunk. Figs. 5 and 6 illustrate well the difference in action between atropine and homatropine in the inhibitory apparatus of the heart in dogs. In these experiments the vagus response was first tested with an induction coil and the amount of energy required to produce the first definite inhibition of the heart was determined. A small dose of atropine was injected and the depressant effect on the inhibitory mechanism was studied with the same induction coil. The amount of atropine required to produce complete paralysis, so that even a maximum stimulation produced no effect, was then determined.

Fig. 5 illustrates a vagus experiment on a dog weighing 12 kilos. The vagi having been dissected out, the electrode of an induction coil was applied to them and the point at which the first response to stimulation occurred was noted. In this experiment such a point was when the secondary coil was 10 cm. distant from the primary. One milligram of atropine sulphate was then injected intravenously. Almost immediately afterwards complete paralysis of the vagus endings occurred so that even the full strength of the induction coil failed to produce inhibition of the heart.

Exactly similar experiments were made with homatropine. As is seen in Fig. 6 it took eight times as much homatropine to completely paralyze the vagus apparatus of the heart. In this experiment a dog weighing 10 kilos was prepared in the same way as in the previous experiment and the vagus was found to be even more sensitive than in the previous dog, the first response to stimulation occurring at the distance of 12 cm. from the primary coil. It required a total of 8 mg. of homatropine in divided doses to produce paralysis of the vagus endings.

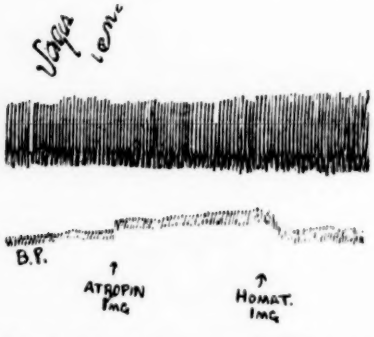


Fig. 7.—Blood pressure and respiratory tracings of dog weighing 10 kilos. Ether anesthesia. One mg. of atropine sulphate produces rise in blood pressure. One mg. of homatropine hydrobromide produces fall in blood pressure.

Fig. 8.—Dog, 8 kilos, paraldehyde anesthesia, decerebration. One mg. of atropine produces rise in blood pressure. One mg. of homatropine produces fall in blood pressure.

In the second place simultaneously with the effect on the inhibitory response of the vagus a very interesting phenomenon was noted. Whereas injections of atropine in moderate doses ordinarily produce a slight rise in blood pressure due to loss of normal heart inhibition, it was noted that after injections of even small doses of homatropine a fall in pressure was produced. Fig. 7 is an illustration of such an experiment. It will be noted that after injecting 1 mg. of atropine in this dog inhibition was paralyzed and as a consequence the blood pressure was slightly increased. On injecting 1 mg. of homatropine, however, a decided fall in pressure occurred in the same animal. This fall in blood pressure was not explainable by a central effect on the brain as the same phenomenon and the same difference between atropine and homatropine were observed in decerebrated animals as illustrated in Fig. 8.

In the third place inspection of the splanchnic viscera in the course of the above experiments revealed, in every case when homotropine was injected, a marked

vaso-dilatation of the abdominal viscera. No such effect was noted after injections of ordinary doses of atropine.

These observations at once point to a difference in action between atropine and homatropine on the vagus mechanism of the heart. A careful examination of the literature on homatropine showed that a number of older observers were not entirely ignorant of this difference in action between atropine and homatropine on the heart. Thus it was already mentioned that de Schweinitz and Hare noted a slowing of the pulse after the administration of homatropine instead of the acceleration usually observed after atropine injections. Bertheau[16] in his study of homatropine noted a slowing of the pulse and stated that excitation of the vagus nerve in animals did not indicate a paralysis of the vagus terminals after homatropine injections. The same author also remarks that homatropine has but little effect in checking the secretions of sweat. Tweedy and Ringer[17] also mentioned the fact that homatropine produces a slowing of the pulse in man and is not effective in checking the secretion of sweat glands. They moreover made experiments with frogs' hearts and noted that homatropine does not antagonize the effects of muscarine on the heart. All these observations led the author to suspect that the action of homatropine is not completely explainable by its effects on the parasympathetic nervous system and to surmise that it might possibly exert an action directly on the muscle cells. Accordingly further experiments were undertaken to decide this point.

COMPARISON OF ATROPINE AND HOMATROPINE ON ISOLATED ORGANS.

Atropine is generally regarded as a powerful antispasmodic and it has been used as such clinically. While its relaxing properties on smooth muscle organs are quite striking they are by no means uniform, for on smooth muscle viscera the antispasmodic effect of atropine varies not only with the dose of the drug but also with the organ studied. Thus, for instance, the author has already shown in another paper that in the case of the isolated ureter small doses of atropine are actually stimulating and not sedative to the contractions and the tonus of the organ.[18] In the present investigation a comparative study of atropine and homatropine was undertaken on excised muscle of various viscera. The following organs were examined: uterus, urinary, bladder, ureters, stomach, intestines, gall bladder and bronchi. The organs were obtained from various animals, namely, dogs, cats, rabbits, guinea pigs, rats, mice; on a few occasions human tissue was procured from the surgical operating room in cases where extirpation of gall bladder and other organs was performed. The action of drugs on the tissues was studied in the ordinary way by suspending the same in oxygenated Locke's solution at body temperature and introducing the chemicals into the solution.

On comparing the effects of homatropine with atropine it was found that while in the case of some organs, especially the intestines, both of the alkaloids acted as very powerful depressant or antispasmodics, in the case of other organs the intensity and rapidity of action was different for the two drugs. Thus, for instance, in the case of the ureter small doses of atropine produced no inhibition of contractions and indeed actually tended to stimulate the same, whereas homatropine acted as an immediate depressant or relaxant, causing cessation of the contractions and lowering of the tonus. Similar results were obtained in the case of the urinary bladder.

In the case of the uterus, by treating the same preparations or two exactly similar preparations with small doses of atropine and homatropine it was quite evident that the antispasmodic or relaxant effect was much greater in the case of homatropine. Whereas in such cases atropine produced a gradual relaxation of the muscle, the effect of homatropine was much more rapid and the relaxation came on abruptly.

In the case of the intestines the difference between the two alkaloids was very slight, inasmuch as atropine in very small doses produces rapid relaxation of the intestinal tonus and inhibition of its contractions. The intestinal effect was studied in this connection not only in excised preparations but also *in situ* in cats and rabbits. It was noted that after injections of minute doses of either atropine or homatropine intravenously, immediate cessation of peristalsis occurred, but in the case of homatropine this was accompanied by a marked *dilatation* of the splanchnic vessels which did not occur in the case of atropine.

The effects of the two drugs were also studied after previous stimulation of the preparations with parasympathetic poisons such as pilocarpine, physostigmine and muscarine. On comparing the results obtained it appeared that these parasympathetic drugs antagonized the effects of atropine much more than those

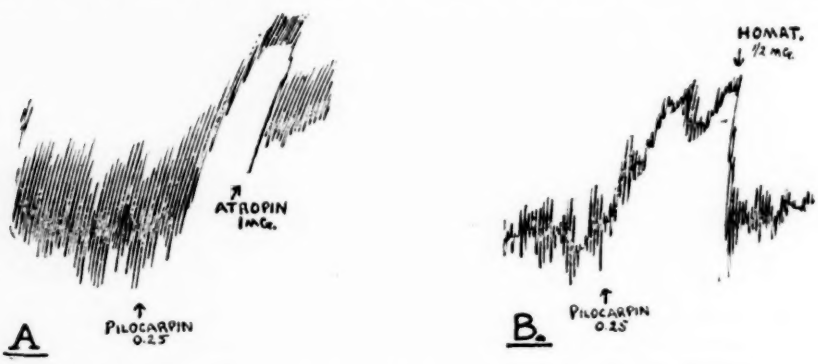


Fig. 9.—Small intestine of cat. A, the effect of pilocarpine and atropine. B, effect of pilocarpine and homatropine.

of homatropine. In other words, after previous construction of smooth muscle preparations with one of the parasympathetic drugs relaxation was produced much more promptly and with smaller doses of homatropine than by the use of atropine. All these observations tended to support the view that homatropine produced relaxation of smooth muscle not exactly through the same mechanism as atropine did. This view was further strengthened by experiments with certain other esters of mandelic acid.

EFFECT OF SOME OTHER MANDELIC ESTERS.

Three other mandelates besides tropine mandelate or homatropine have been introduced into therapeutic practice. These are antipyrine mandelate, known as tussol, eucaine mandelate, extensively employed under the name of euphthalmine, and a combination of phenetidine with mandelic acid, marketed under the name of amygdophenine. The author was unable to obtain a sample of amygdophenine but did procure specimens of tussol and euphthalmine. The action of these was

studied on various smooth muscle preparations and compared with those of antipyrine and eucaine themselves. The results obtained are illustrated in the subjoined figures and were most remarkable. It was found that whereas solutions of antipyrine or of eucaine themselves when administered in moderate doses produced

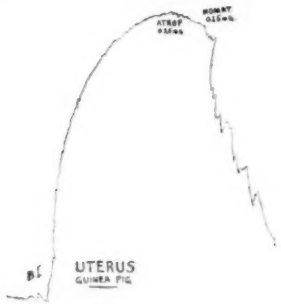


Fig. 10.—Uterus of guinea pig. Stimulation with histamine (B-I) followed by atropine, 0.25 mg., and homatropine, 0.25 mg.

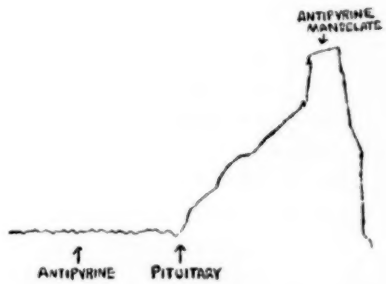


Fig. 11.—Uterus of guinea pig. Effect of antipyrine, pituitary and antipyrine mandelate.

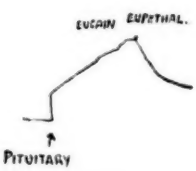


Fig. 12.—Uterus of guinea pig. Contracted by pituitary extract. Eucaine has no effect. Euphthalmine (eucaine mandelate) produces relaxation.

Fig. 13.—Strip of intestinal muscle of cat contracted by pilocarpine hydrochloride, 1 mg., and relaxed by 5 mg. of ethyl mandelate in 40 cc of Locke's solution.

Fig. 14.—Uterus of guinea pig. Fifty cc of Locke's solution. 1, effect of pituitary extract; 2, effect of sodium tropate, 3 mg.; 3, effect of tropine hydrochloride, 3 mg.; 4, effect of atropine sulphate, 2 mg.; 5, effect of pituitary extract, 0.25 cc; 6, effect of homatropine hydrobromide, 2 mg.

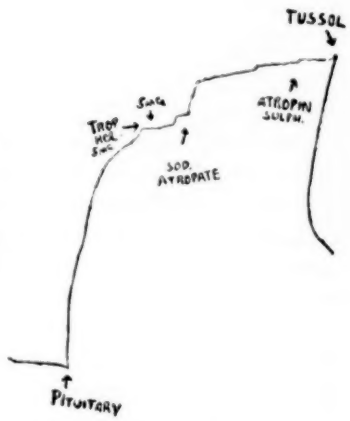


Fig. 15.—Uterus of guinea pig. Contracted by pituitary fluid. Tropine hydrochloride has no effect. Sodium atropate has no effect. Atropine sulphate has no effect. Tussol (antipyrine mandelate) produces no relaxation.

no antispasmodic or sedative effect on the muscle preparations, the introduction of even small doses of the mandelic esters of the same was followed by an immediate and abrupt relaxation, comparable very much to the powerful relaxing effects produced by the alkaloid papaverine.

The author was fortunate in securing a specimen of pure ethyl mandelate (Kahlbaum). Experiments with this simple ester also revealed that it was a powerful relaxant of smooth muscle. The above experiments with various mandelic acid esters obviously indicated that the mandelic acid radical plays an important rôle in their antispasmodic influence on smooth muscle preparations. Figs. 9–13 serve to illustrate the findings just described.

Fig. 9 illustrates an experiment on two segments of the small intestine of a cat. At A the intestine is stimulated by 0.25 gram of pilocarpine hydrochloride and afterwards treated with 1 mg. of atropine sulphate. At B intestine is stimulated with the same quantity of pilocarpine hydrochloride and afterwards with 0.5 mg. of homatropine hydrochloride. It will be noted that the homatropine produces the greater relaxation.

In Fig. 10 an experiment on the isolated uterus of a virgin guinea pig was performed. This was first stimulated to powerful contraction by a small dose of histamine which brought the uterus into a state of tonic contraction. At the height of the contraction 0.25 mg. of atropine sulphate was introduced into the solution and was followed by practically no effect. The same quantity of homatropine solution was then introduced and as will be noted was followed by an immediate and rapid relaxation of the organs.

In Fig. 11 another uterine preparation from a guinea pig was treated with antipyrine without previously being stimulated by an oxytocic and showed no change. It was then contracted with a few drops of pituitary liquid and at the height of its contraction 5 mg. of antipyrine mandelate caused immediate relaxation and fall of the tonus below the original level.

Fig. 12 illustrates an experiment in which a uterus was first contracted with pituitary and then treated with a solution of eucaine (5 mg.). No effect was produced. On adding, however, the same quantity of eucaine mandelate (euphthalmine) relaxation occurred.

Fig. 13 shows a curve traced by a bit of circular muscle of cat's intestine. This was stimulated to contraction by 1 mg. of pilocarpine in 50 cc of Locke, and was relaxed by the introduction of 5 mg. of ethyl mandelate in the same solution.

EFFECT OF SOME DECOMPOSITION PRODUCTS.

In order to analyze still further the rôle played by mandelic acid in the action of homatropine, experiments were undertaken with the "Bausteine," or decomposition products of homatropine, on the one hand, and of atropine on the other. In other words, an examination was made of the individual properties of tropine in the form of a simple salt, such as tropine hydrochloride; of tropic acid in the form of sodium tropate; and of mandelic acid in the form of simple salts such as those of sodium and potassium.

It was found that tropine itself when administered in the form of tropine hydrochloride produces very little effect on the tonus or contractions of smooth muscle. Tropic acid itself in the form of its simple salts such as sodium tropate was also found to be very little active in this respect. Moderate quantities of sodium tropate produced no effect on smooth muscle while very large doses of the same only occasionally produced a very slight relaxation of the tonus of a uterus previously brought into a state of maximum contraction by a powerful stimulant

such as pituitary extract. Neither did atropic acid in the form of sodium atropate produce any effect on the behavior of isolated smooth muscle preparations.

On testing the properties of sodium mandelate, however, a very different result was obtained. It was seen at once that sodium mandelate produced a relaxation of tonus and inhibition of the rhythmic contractions of smooth muscle. This was found to be true of preparations from all kinds of organs.

Simple mixtures of sodium tropate with tropine hydrochloride did not produce the same effect as atropine; in other words, it was evident that the action of the atropine molecule was due to an intimate chemical combination of the two components. Simple mixtures of tropine hydrochloride with sodium mandelate, on the contrary, did produce relaxation of smooth muscle preparations. As a result of all these experiments with the components of atropine and homatropine it seemed plausible to assume that the mandelic acid played an important rôle in the antispasmodic properties of homatropine. It was therefore of especial interest to inquire whether that held true for the mydriatic action of homatropine. Accordingly some experiments were carried out to clear up this question.

Fig. 14 shows a uterus of a guinea pig brought into powerful contraction by a drop of pituitary fluid at 1. At 2, 3 mg. of sodium tropate were introduced without any effect; at 3, 3 mg. of tropine hydrochloride, without any effect. At 4, 2 mg. of atropine sulphate produced a slight relaxation. The uterus was stimulated at 5 by a second dose of pituitary. At 6, 2 mg. of homatropine hydrochloride were introduced and this was followed by rapid and marked relaxation of the preparation. In Fig. 15 the uterine horn of a guinea pig was stimulated with pituitary extract. The dose was repeated with the same results. Ten mg. of sodium atropate produced no relaxation and indeed were followed by further contraction of the uterus. Two mg. of atropine sulphate produced no relaxation. Finally 5 mg. of antipyrine mandelate produced an immediate fall of the lever.

ANALYSIS OF HOMATROPINE MYDRIASIS.

The mydriasis produced by homatropine has been studied clinically by many authors, beginning with Völckers and Quincke who first demonstrated it for Ladenburg. The effects of homatropine on the eye were investigated by Bertheau, Tweedy and Ringer, Oliver,[19] Reily,[20] Jackson,[21] Schell,[22] Ziem,[23] Vossius[24] and others. It was established that homatropine produces satisfactory mydriasis but must be used in about double the concentration of atropine and that the mydriasis is of much shorter duration, a circumstance which is clinically usually very desirable. It is also generally conceded that atropine paralyzes accommodation much more quickly and in weaker dilutions than homatropine.

The effect of light in relation to atropine and homatropine has been noted by various authors. Ordinarily exposure to a bright light produces a reflex contraction of the iris. This reflex contraction fails to appear after instillation of full therapeutic doses of atropine. The explanation of this phenomenon is found in the paralysis of the occulomotor nerve terminals supplying the circular muscle of the iris, so that the reflex arc is incomplete and cannot respond to the stimulation of light. When the reaction of the pupil to light is tested after instillation of homatropine, however, this reflex myosis or contraction of the pupil is generally not completely obliterated unless very strong solutions of the alkaloid are employed or weaker solutions repeatedly instilled, for a protracted period of time. The

present author has repeatedly instilled solutions of atropine sulphate (1–1000) and of homatropine (1–500) into the conjunctival sacs of cats and rabbits and found that while the atropine completely obliterated the light reflex, the homatropinized animals still responded with a distinct contraction to the pupil on exposure to a bright light. This difference in the action of the two alkaloids would seem to speak in favor of a different mechanism in the two cases as regards the production of mydriasis. If homatropine were to produce relaxation of the constrictor pupilae by a direct action on the muscle cells without affecting the parasympathetic nerve terminals, then it is easily conceivable how a strong stimulation by light would still produce a contraction of the pupil by reflex stimulation of these nerve terminals. On the other hand, if a drug like atropine completely paralyzes the parasympathetic nerve endings, then no degree of intensity or light stimulation will be able to produce a myosis through a reflex stimulation, no more than the strongest electric stimulation may be able to inhibit the heart action after the vagus nerve terminals in the heart have been paralyzed by atropine.

In order to ascertain further the mechanism of pupillary dilatation produced by homatropine, experiments were made by the author with tropine hydrochloride, sodium tropate, sodium atropate and various mandelic esters. The author was able to confirm the results by Fraser and other earlier investigators with tropine on the eye. Instillation of solutions of tropine hydrochloride into the eyes of cats and rabbits failed to produce mydriasis. Experiments made on excised frogs' eyes gave the same results, tropine hydrochloride produced neither mydriasis nor myosis of the eye.

Tropic acid in the form of its sodium salt was also found to have practically no effect on the pupils of both rabbits and cats and on excised frogs' eyes. On the other hand experiments with ethyl mandelate made by instilling solutions of the same (2 percent) into the eyes of cats and rabbits were found to produce a distinct dilatation. Finally a solution of sodium mandelate was prepared and the same was tested on intact animals and on excised frogs' eyes and it was found that this drug produced a distinct though mild mydriasis or dilatation of the pupil. Thus, for instance, a 4 percent solution of sodium mandelate instilled into rabbits' eyes was followed by a distinct dilatation. A 10 percent solution of the same salt produced a more striking effect.

In conclusion, the action of homatropine and the various related compounds mentioned above were studied on the eye by a new method which, so far as the author is aware, has not been described. The author studied the effects of the various drugs on the *excised* circular muscle of the iris. The eyes of cats, rabbits, dogs and pigs were used in this connection, the cat's eye being the most suitable. The circular muscle of the iris was carefully dissected out, care being taken not to injure it by pulling or tearing, and a suspension preparation was made in the same way as other smooth muscle preparations are studied. When such a preparation is carefully made and the muscle lever is delicately balanced, the iris writes a horizontal line on the hymograph, sometimes exhibiting small rhythmic contractions. The response of the muscle to drugs is then studied by introducing solutions of the same into the suspension chamber. In this way it was found that the muscle contracted after pilocarpine and eserine and relaxed to atropine and homatropine. On studying the effects of tropine, tropic acid, and mandelic acid it was found

that whereas sodium tropate and tropine hydrochloride produced no effect, sodium mandelate and other mandelic esters produced a relaxation of such iris muscle preparations. Furthermore, it was found in some instances that after contracting such preparations with pilocarpine and relaxing the same with atropine on subsequent addition of homatropine an even greater relaxation of the muscle could be produced.

In Fig. 16, the isolated circular muscle of the iris of the cat was suspended in oxygenated Locke's solution. On the addition of 2 mg. of pilocarpine in 50 cc of Locke contraction occurred. One mg. of atropine failed to relax the preparation. The addition of 1 mg. of homatropine, however, produced a marked and rapid relaxation.

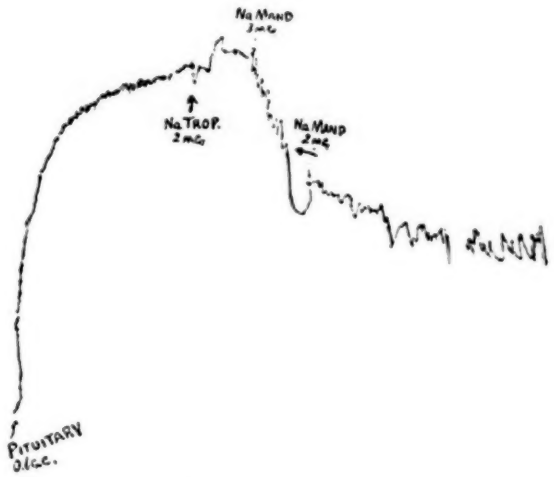


Fig. 16.—Uterus of guinea pig. Contraction after 0.1 cc of pituitary fluid. Sodium tropate, 2 mg., has no effect. Sodium mandelate, 3 mg., produces relaxation.

Fig. 17.—Isolated circular muscle of the iris from a cat. Pilocarpine, 2 mg., in 40 cc of Locke produces contraction. Atropine sulphate, 0.25 mg., has little effect. Homatropine hydrobromide, 0.25 mg., produces relaxation.

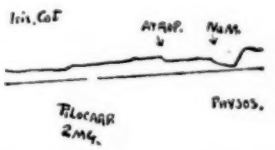


Fig. 18.—Iris preparation same as above. Contraction after pilocarpine, slight relaxation by atropine, greater relaxation by sodium mandelate and second contraction after physostigmine.

In Fig. 17 the circular muscle of the iris of a cat was first stimulated by pilocarpine and this contraction was antagonized by 1 mg. of atropine sulphate. On addition of 5 mg. of sodium mandelate a much more marked relaxation occurred than after the atropine. The fact that the preparation was not injured by the mandelate is indicated by a subsequent response to physostigmine.

DISCUSSION.

The analysis of the results of the various experiments by the author enumerated above justified the formulation of some plausible generalizations and the drawing of certain conclusions. It is evident, in as far as the effect on the viscera is

concerned, that the antispasmodic effect of atropine on smooth muscle is due to a specific and peculiar action of the atropine molecule as a whole on the myoneural junctions of the parasympathetic nervous system, because neither tropine (tropine hydrochloride) nor tropic acid (sodium tropate), nor simple mechanical mixtures of the two produce any such effect. Very different, however, are the properties of homatropine in this respect. While large doses of homatropine do paralyze the vagus endings on the heart and for the production of such paralysis the homatropine molecule as a whole is necessary, the inhibitory and tonus lowering properties of homatropine on smooth muscle can in a measure be produced by one of its component nuclei, namely, by the mandelic acid radicle. Thus the vaso-

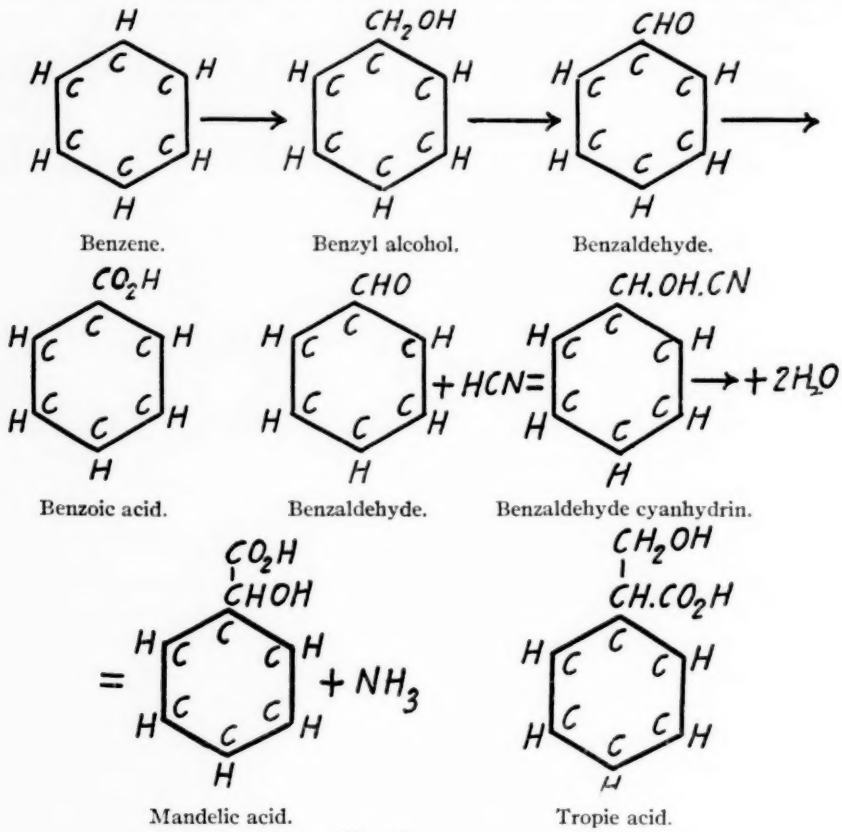


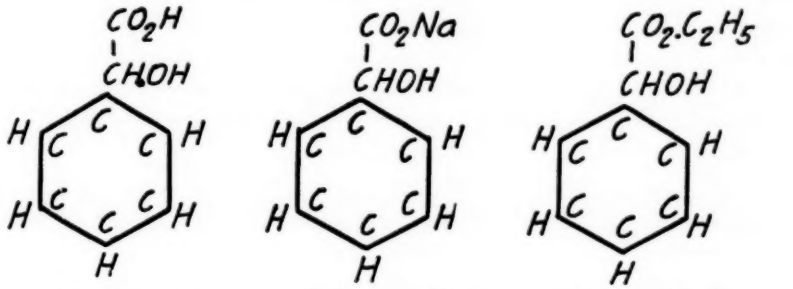
Fig. 19.

dilatation and consequent fall in blood pressure, and the relaxation of uterine, intestinal, vesical and other smooth muscle preparations are produced by various esters of mandelic acid and also by the simple sodium and potassium salts of mandelic acid. The conclusion is therefore justifiable that this property of homatropine in relation to smooth muscle is inherent to a great extent in its mandelic component.

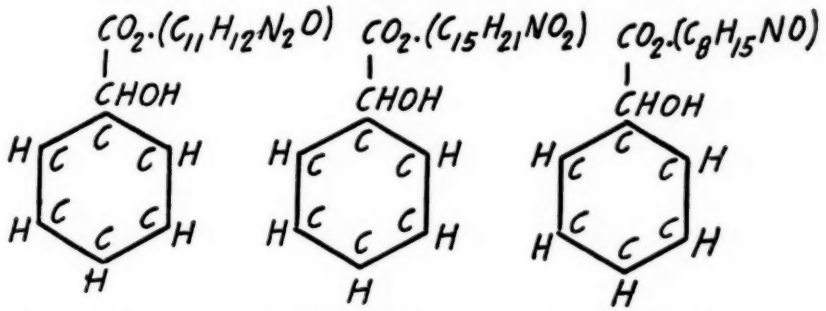
A careful examination of the action of homatropine as compared with atropine especially in regard to their antagonism to various parasympathetic pressor drugs, such as muscarine, pilocarpine and physostigmine, would seem to indicate that the muscle effect of homatropine is not exerted through the parasympathetic

terminal apparatus. The behavior of other mandelic esters and of sodium and potassium mandelates renders this view even more conclusive. Neither is there any evidence as far as the author is aware, pointing to the true sympathetic nervous mechanism as being responsible for the antispasmodic effects of these substances. All the evidence on hand seems to speak in favor of the action being very much the same as that of the alkaloid papaverine and also of certain benzyl esters and benzyl alcohol, which the author has shown to act in the same way as papaverine.[18,19] This action is probably exerted *directly on the muscle cell.*

The interesting properties of various mandelates described above are not altogether unexpected in view of the remarkable properties of various benzyl compounds which have been discovered by the author. The subjoined structural



Mandelic acid. Sodium mandelate. Ethyl mandelate.



Antipyrine mandelate (tussol). Eucaine mandelate (euphthalmine). Tropine mandelate (homatropine).

Fig. 20.

formulas will serve to show the closer relationship of mandelic acid to benzaldehyde which has already been investigated by the author and shown to act as an antispasmodic (Fig. 18). It will be seen that mandelic acid is prepared from benzaldehyde by first treating with hydrocyanic acid and thus forming benzaldehyde cyanhydrin. Fig. 20 exhibits the structural formulas of sodium mandelate, ethyl mandelate and other mandelic esters. Fig. 19 also indicates the structure of tropic acid and the comparison of this formula with that of mandelic acid will reveal at once that mandelic acid is much more closely related to benzaldehyde and benzyl alcohol than tropic acid is.

In view of the above considerations it would seem probable that the mydriatic action of homatropine is produced in part at least by a direct action on the muscle of the iris without the mediation of the parasympathetic terminal nervous appara-

tus. This is further corroborated by the difference in the response to light stimulation which has already been described and also by the experiments on isolated iris muscle shown by the author.

This peculiar action of homatropine on smooth muscle is supported by the careful observations of clinical ophthalmologists. It has been noted by Jackson and others that instillation of homatropine into the conjunctional sac is followed by a hyperemia of the conjunctival and corneal vessels. This is not regarded as due to an irritant effect of the drug but rather in the nature of a true hyperemia or vaso-dilatation. To quote literally from the excellent paper of E. Jackson we read, "there is hyperemia of the eye due to enlargement of minute vessels that form a rosy zone around the cornea, the straight vessels and the deep vessels of the sclerotic. This is not due to water or to acid. I believe it to be due to a specific influence of the drug on the vessels." This careful observation of a keen clinician is in perfect agreement with the experimental results obtained with atropine which has been found by the author to be a vaso-dilator due to its antispasmodic or relaxing effect on the muscle of the vessel walls.

SUMMARY.

1. A comparative study of the pharmacological properties of atropine and homatropine and their products of decomposition was made on the circulation, the eye, and all kinds of smooth muscle viscera.

2. While small doses of atropine completely paralyze the vagus terminals in the heart, and through a loss of normal vagus inhibition this generally causes a rise in blood pressure, equivalent and even larger doses of homatropine fail to paralyze these vagus endings, and cause a fall in blood pressure due to a marked vaso-dilatation.

3. Homatropine as compared with atropine is a more powerful drug in respect to the inhibition of contractions and lowering of the tonus of smooth muscle preparations.

4. Of the components of atropine, neither tropine, nor tropic acid alone, or a simple mixture of their salts produces the characteristic effects of atropine on smooth muscle.

5. Of the components of the homatropine molecule, mandelic acid in the form of simple salts or esters exhibits the characteristic effects of homatropine on smooth muscle.

6. As a conclusion from the data obtained it would seem that the property of relaxing smooth muscle and especially of producing mydriasis resides chiefly in the mandelic component of the homatropine molecule, and is probably produced through a direct action on the muscle cells.

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A PHARMACOLOGICAL EXAMINATION OF BENZALDEHYDE AND MANDELIC ACID.*

BY DAVID I. MACHT.†

INTRODUCTION.

About five years ago the author first published his studies on the relationship between the chemical structure of the opium alkaloids and their pharmacological action on smooth muscle.[1] He showed that in this respect the principal alkaloids of opium can be sharply divided into two groups, the pyridine-phenanthrene group of which morphine is the principal member and the benzyl-isoquinolin group of which papaverine is the principal representative. It was further shown that a peculiar and characteristic property of papaverine as a relaxant of smooth muscle was due to the benzyl nucleus of its molecule. As a result of this pharmacodynamic analysis the discovery of the remarkable antispasmodic properties of the benzyl esters, benzyl benzoate, benzyl acetate, etc., followed. Almost simultaneously with the publication of the author's studies concerning benzyl esters the author also announced the discovery of the local anesthetic properties of benzyl alcohol.[2] The pharmacological and therapeutic properties of the benzyl esters and benzyl alcohol have been described in various publications by the author himself and by other investigators. A very good summary of the work to date appeared in Merck's "Jahresberichte" for 1921.

In connection with the study of benzyl esters and benzyl alcohol it was logical to inquire into the pharmacological and physiological effects of benzaldehyde. A preliminary communication on the subject by the author appeared some time ago.[3] In the present paper it is proposed to report more fully the author's investigations on the subject.

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* The expenses of this investigation have been supported in part by a grant from the Research Fund of the American Pharmaceutical Association.

† From the Pharmacological Laboratory, Johns Hopkins University.

CHEMISTRY.

Benzaldehyde, $C_6H_5.CHO$, is a constituent of a number of natural volatile oils. It occurs in various amounts in a number of plants, especially those belonging to the family of *rosaceae* and more particularly in the species *prunus*. Thus it is found in the cherry laurel or *prunus laurocerasus*, in *prunus persica* or peach kernels, in *prunus serotina*, in *prunus puddum*, *prunus cerasus*, *prunus domestica* and *prunus spinosa*. Benzaldehyde is an important constituent of *amygdala amara* or bitter almond. It is also found in small quantities in some species of *cinnamomum*, *genista*, *myristica*, in the *balsam* of *tolu* and in *benzoinum*. Perhaps the most important natural source of benzaldehyde is oil of bitter almonds. As is well known benzaldehyde is formed from the glucoside amygdalin by the action of the enzyme emulsin, each molecule of amygdalin by yielding one molecule of hydrocyanic acid and one molecule of benzaldehyde, with two molecules of dextrose.

Benzaldehyde was first prepared by Liebig and Wöhler in 1837 who ascertained its composition and studied its relation to benzoic acid. Having been first isolated from the oil of bitter almonds it was originally designated pharmaceutically as *oleum amygdalarum aethereum sine acido prussico*. Benzaldehyde can be prepared (*a*) from bitter almond oil, and (*b*) from toluene. The artificial benzaldehyde can be prepared from toluene in two ways; in one case the toluene is first converted into benzyl chloride, this is heated with barium nitrate and water while passing a current of carbon dioxide through the mixture. The benzyl nitrate resulting decomposes with the formation of benzaldehyde and oxides of nitrogen. Another method is to convert toluene into benzal chloride which can be transformed directly into benzal glycol, $C_6H_5CH(OH)_2$. On treating the benzal glycol with caustic soda or milk of lime or with water under pressure benzaldehyde is directly formed.

Benzaldehyde is a colorless or yellowish, strongly refractive liquid. It possesses the odor peculiar to oil of bitter almonds and a burning aromatic taste. Its specific gravity is about 1.045 at 25 degrees C. and its boiling point is 178–182 degrees C. It is optically inactive. It is sparingly soluble in water, the solution being about 1–300 but is readily soluble in most organic solvents and also in oils. When exposed to oxygen it is readily oxidized to benzoic acid. In the pharmacological experiments performed in this investigation a solution of 1–500 or 0.2% was easily prepared and used.

PHARMACOLOGICAL PROPERTIES.

Inasmuch as the benzyl esters, such as benzyl benzoate and benzyl acetate, are most remarkable for their antispasmodic action on smooth muscle and inasmuch as the most striking characteristic of benzyl alcohol is its local anesthetic property, it was interesting to inquire into the pharmacological behavior of benzaldehyde from these two points of view. Furthermore the author has called attention elsewhere to the fact that benzyl alcohol in addition to its striking local anesthetic effect possesses also to quite a marked degree antiseptic properties as indicated by its action on a number of bacteria.[4] It was therefore of interest also to inquire into the possible antiseptic properties of benzaldehyde.

Effect on Smooth Muscle.—Experiments were made on the isolated muscle preparations from the uterus, intestines, stomach, urinary bladder, gall bladder,

ureters, vas deferens, seminal vesicles, uterus, bronchi and arteries taken from various animals, namely, dog, cat, rat, rabbit, mouse, guinea pig, pig, frog and in a few cases experiments were also made on the isolated muscle from human tissue obtained from the surgical operating room. All these experiments indicated that benzaldehyde is a marked antispasmodic exerting the same effect as the benzyl esters already studied by the author. In these experiments *in vitro* the author

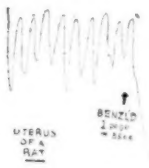

Fig. 1.—Uterus of rat. One drop of benzaldehyde in 35 cc of Locke produces marked relaxation.

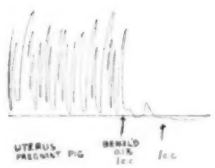

Fig. 2.—Uterus of pregnant pig. One cc of 0.1% solution of benzaldehyde in 50 cc of Locke's solution produces inhibition of contraction.

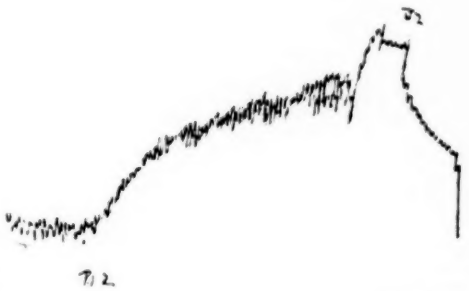

Fig. 3.—Jejunum of guinea pig stimulated by 1 mg. of pilocarpine hydrochloride and relaxed by 1 drop of benzaldehyde in 50 cc of Locke's solution.

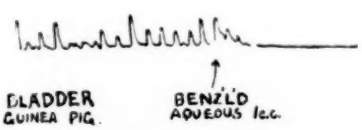

Fig. 4.—Urinary bladder of guinea pig. Inhibition produced by 1 cc of 0.1% solution of benzaldehyde in 30 cc of Locke.

Fig. 5.—Ureter of pig. In 30 cc of Locke's solution effect of 2 cc of 0.2% benzaldehyde.

used for the most part a solution of benzaldehyde in water or in physiological sodium chloride, 1–500. The results obtained are illustrated by the subjoined figures.

Fig. 1 shows the effect of benzaldehyde on the contractions of a horn of a uterus of a rat. The preparation was suspended in 35 cc of Locke's solution; one small drop of benzaldehyde was introduced into the chamber. Note marked relaxation and inhibition of contraction.

Fig. 2 shows the effect of benzaldehyde on a bit of uterus from a pregnant sow. In this case 1 cc of a 0.1% solution of benzaldehyde was sufficient to produce a marked relaxation and inhibition of contraction.

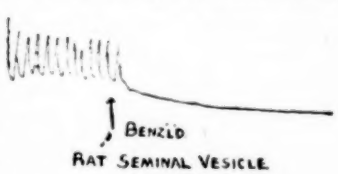

Fig. 6.—Seminal vesicle of rat. Relaxation produced by 1 cc of 0.2% solution of benzaldehyde in 30 cc of Locke.

Fig. 3 shows the effect of 1 drop of benzaldehyde introduced into a chamber containing 50 cc of Locke's solution in which a short loop of jejunum from a guinea pig was suspended. Notice relaxation.

Fig. 4 shows the effect of benzaldehyde on the isolated bladder of a guinea pig. One cc of a saturated solution of benzaldehyde in 35 cc of Locke's solution produced inhibition.

Fig. 5 shows the effect of 2 cc of 0.2% solution of benzaldehyde on the contractions of the ureter of a pig.

Fig. 6 shows the effect of 1 cc of 0.2% solution of benzaldehyde on the contractions and tonus on the seminal vesicle of a rat.

In experiments with benzaldehyde *in vitro* it is important to bear in mind that dilute solutions of it very rapidly oxidize, forming benzoic acid, and this increase in the hydrogen-ion concentration of the solution sometimes produces anomalous results. The experiments must be made with solutions of benzaldehyde *freshly prepared* immediately before the experiment.

Fig. 7.—Effect of benzaldehyde on the respiration and blood pressure of cat. Upper curve indicates respiration, lower curve indicates blood pressure.

The effect on various organs *in situ* was also studied to some extent, especially on the intestines and blood pressure. In these experiments again care must be taken to discount the anomalous effects produced by oxidized solutions of benzaldehyde and it must be furthermore borne in mind that the sedative effects of benzaldehyde as well as those of the benzyl esters come on slowly and run parallel to the hydrolysis or decomposition of those compounds in the body. After injecting solutions of emulsions of benzaldehyde in rabbits and other animals a marked paresis or relaxation of the intestines and the urinary bladder with marked vaso-dilatation of the splanchnic vessels is noted at the expiration of ten or more minutes after injection and sometimes earlier. Fig. 7 is a striking illustration of the effect of benzaldehyde on the blood pressure. In this experiment a cat weighing 2.5 kilos was anesthetized with urethane. Note the effect of injection intravenously of 4 cc of a 0.5% solution of benzaldehyde, as manifested by a fall in blood pressure and showing of the respiration.

Anesthetic Effect.—The anesthetic action of benzaldehyde can be readily demonstrated by all of the common methods employed in experimental pharmacology. The author studied pure benzaldehyde itself and also aqueous solutions of the strength of 1–500. Pure benzaldehyde can be shown to produce blocking of nerve impulses in the sciatic nerves of cats and dogs paralyzing the ascending or sensory fibers before the descending or motor fibers of the nerve trunk. Conduction anesthesia was also found by the author to take place by applying even weak solutions of benzaldehyde, 1–500, to the sciatic nerves of frogs.

The dilute solutions of benzaldehyde were studied for anesthesia on the eyes of rabbits and dogs and on the skin of frogs. The author found on instilling a solution of 1–500 into the conjunctival sac that complete anesthesia occurred at the end of two minutes and lasted for some ten to fifteen minutes. Together with the anesthesia of the cornea considerable irritation of the conjunctiva occurred, due probably to the gradual oxidation of the benzaldehyde with the formation of benzoic acid.

The anesthetic action on frogs' skin was strikingly demonstrated by the well-known method employed in pharmacological laboratories. Frogs were suspended with the brain destroyed but the spinal cord intact. The response of the legs on dipping in a dilute solution of sulphuric acid or hydrochloric acid was determined. One of the legs was then immersed for periods varying from one to two to five minutes in solutions of benzaldehyde of 1–500. On subsequent testing with the same chemical stimuli, that is, solutions of acids, no reflex contraction of the leg could be elicited, thus indicating an anesthesia or paralysis of the sensory nerve endings. This anesthetic effect persisted for half an hour and longer. As a result of the various experiments on anesthesia there was no doubt that benzaldehyde exerted a local anesthetic action very much like benzyl alcohol with the sole difference that while benzyl alcohol is fairly stable when kept free from alkalis, as shown by Macht and Scholl,[4] benzaldehyde rapidly oxidizes to benzoic acid and is therefore unsuitable for practical use as a local anesthetic, especially on mucous surfaces such as those of the eye.

ANTISEPTIC ACTION.

The author in collaboration with Drs. Satani and Schwartz[5] has already called attention to the antiseptic and germicidal properties of benzyl alcohol, for *B. coli;* staphylococcus, and gonococcus. It was interesting to inquire into whether benzaldehyde exhibited similar effects. Accordingly a series of bacteriological experiments were carried out for the author by Miss J. H. Hill.

In testing the drug, the benzaldehyde was diluted with cottonseed oil. It was found that pure benzaldehyde diluted with an equal part of oil killed *B. coli* in less than one minute. Benzaldehyde one part mixed with parts of oil also killed the bacteria in one minute. A dilution of one in a hundred killed an enormous number of the organisms in one hour, and destroyed all of them within three hours.

It is thus evident that benzaldehyde possesses distinct germicidal properties.

TOXICOLOGY.

The toxicity of benzaldehyde is very similar to that of benzyl benzoate, benzyl alcohol and benzyl succinate[6] which have already been studied by the author. In other words the toxicology of benzaldehyde is very low. Experiments on rats show that the lethal dose of pure benzaldehyde was about 0.5 cc per 100 grams weight of the animal when injected subcutaneously. The same dose injected intraperitoneally produced marked poisoning but was occasionally recovered from. In dogs 1 cc pure benzaldehyde injected intravenously or subcutaneously produced a slight slowing of the respiration but otherwise no deleterious result. On administering pure benzaldehyde mixed with a little water to dogs by stomach tube 2 cc of pure benzaldehyde per kilo produced no effect with the exception of a slight slowing of the respiration. On intravenous injection the author has been able to administer to rabbits a solution of benzaldehyde in normal saline of 0.2% strength in doses as high as 20 cc per kilo weight of the animal without dangerous results. Intravenous injection of such aqueous or saline solutions in dogs were given even in larger doses without any harm, the only results noted in anesthetized animals being a lowering of the blood pressure, a slight slowing of the respiration and an inhibition of the intestinal contractions with vaso-dilatation of the splanchnic vessels.

When very large doses of benzaldehyde are injected into animals the most important toxic effects are exerted on the medulla. Respiration is slowed and after very large doses is paralyzed. The heart is very little affected by benzaldehyde, after intravenous or other injections in the intact animal. On the isolated frog's heart benzaldehyde acts as a muscular depressant.

EXAMINATION OF MANDELIC ACID.

Closely related to benzaldehyde and occurring to some extent in nature is mandelic acid. Mandelic acid is chemically *phenylglycolic* acid with the formula $C_6H_5.CHOH.CO_2H$. The relation of this acid to benzaldehyde is very close and it can be prepared from the latter by first treating benzaldehyde with hydrocyanic acid, forming benzaldehyde cyanhydrin. This on treatment with water forms ammonia and phenylglycolic acid.

Mandelic acid is a colorless substance which crystallizes in platelets melting at 115–118° C. It is freely soluble in water, alcohol and ether and easily forms salts or esters. On oxidation it is transformed into benzoic acid. According to Schulze and Graebe[7] mandelic acid in the body is metabolized and excreted as hippuric acid.

Owing to the close relationship of mandelic acid to benzaldehyde it was interesting to inquire into its pharmacological properties which, so far as the author is aware, have never been investigated. For this purpose sodium and potassium mandelates were employed and later the ester ethyl mandelate and some more complex esters were also experimented with. It was found that ethyl mandelate and to a somewhat lesser degree sodium and potassium mandelates exhibited the characteristic antispasmodic properties of the benzyl esters, benzyl alcohol and benzaldehyde, on smooth muscle. Ethyl mandelate and sodium mandelate were found to relax smooth muscle preparations and in blood-pressure experiments they were found to lower the blood pressure through a marked vasodilatation of the splanchnic vessels, and also to produce broncho-dilatation. These antispasmodic properties are exhibited in even a higher degree in certain more complex esters of mandelic acid and are of great pharmacological interest. The author is conducting an investigation with a number of these bodies and the results of the work are to be published in a separate paper. Suffice it to say that the pharmacological properties of mandelic acid shed a new light on the physiological effects of the well-known mydriatic, homatropine, as demonstrated by the author elsewhere. (Fig. 8.)

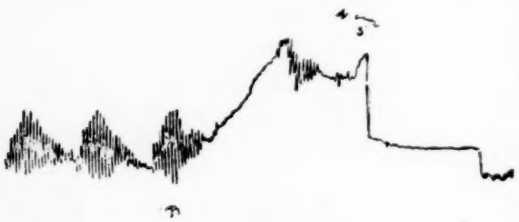

Fig. 8.—Jejunum of rabbit. Stimulation with 1 mg. of pilocarpine hydrochloride in 40 cc of Locke and relaxation of the same on introduction of 5 mg. of sodium mandelate.

DISCUSSION.

An analysis of the data obtained from the pharmacological study of benzaldehyde reveals the fact that this substance can no longer be regarded as a mere aromatic or flavoring agent. While the toxicity of benzaldehyde is comparatively very low it exhibits certain very striking pharmacodynamic effects, the most important of which are of a threefold nature. The substance possesses important

antispasmodic, local anesthetic and *antiseptic* properties all of which are exhibited not only by pure benzaldehyde but even by weak solutions of it in alcohol, oil or water. These characteristic effects of benzaldehyde considered in connection with the similar properties of benzyl alcohol and certain benzyl esters such as benzyl benzoate and benzyl acetate throw a new light on certain well-established empirical therapeutic uses of old drugs. A good example of such an empirical practice is the use of benzoinum in the form of a simple or compound tincture of benzoin. These preparations have long ago been found useful as sedatives in sore throat and also as antipruritics in cases of skin irritation. With the rise of modern pharmacology there was a tendency on the part of some writers to taboo these empirical usages without any further experimentation and to ascribe the beneficial effects of benzoin, if any, to psychic suggestion or in the case of inhalation to the beneficent effects of steam. In view of the present investigation a rational basis for the empirical use of benzoin is found. The author has made mixtures of water with tincture of benzoin in proportions of 1 to 10 and even weaker concentrations, and distilled these mixtures collecting the distillate through a condenser. On testing the distillate he was able to show that there is a sufficient amount of benzyl alcohol and benzaldehyde present in the fluid obtained to demonstrate a definite anesthetic effect on frog skin. Again bearing in mind the anesthetic and also antiseptic properties of benzyl alcohol and benzaldehyde and related compounds the use of such in lotions for itching and burning of the skin is evidently also justified on pharmacological grounds.

It has been found that a combination of antipyrine with mandelic acid in the form of an ester, antipyrine mandelate, or *tussol*, is beneficial in certain cases of whooping cough. Such a therapeutic effect with such an ester would seem to be a plausible one in view of the experiments by the author with benzyl benzoate in the same clinical condition.[8] The above experiments with benzaldehyde suggest, furthermore, an improvement in the therapeutic practice in the case of inhalations and other applications of benzyl compounds in that such preparations can be rendered more efficient by fortifying them with an addition of benzaldehyde or benzyl alcohol.

SUMMARY.

1. A pharmacological study of benzaldehyde showed that while the substance is of low toxicity it exhibits three important physiological effects.

2. Benzaldehyde was found to relax the tonus and inhibit contractions of smooth muscle.

3. Benzaldehyde was found to possess definite local anesthetic properties.

4. Benzaldehyde was found to exhibit a distinct antiseptic effect on bacteria.

5. Mandelic acid closely related to benzaldehyde chemically was found to possess distinct antispasmodic properties as exhibited by a study of its salts and esters.

6. The interesting properties of benzaldehyde and mandelic acid shed light on the beneficent results obtained by the empirical use of certain natural drugs containing benzyl compounds.

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COMPOSITION OF NECTANDRA COTO, RUSBY NOV. PRELIMINARY REPORT.

BY HARVEY A. SEIL.

Previous investigators have shown[1] that true coto bark contains cotoin, cotoin methyl ethers, phenyl coumalin, protocotoin, methyl-protocotoin, ethereal oil and tannin. The chemical constitution of cotoin and its derivatives has been carefully studied and can be briefly outlined as follows:

Cotoin—$C_6H_5.CO.C_6H_2(OH)_2.OCH_3$. Melting point, 130° C.

Hydrocotoin
(Cotoin monomethyl ether)—$C_6H_5.CO.C_6H_2(OH)(OCH_3)_2$. Melting point, 98° C.

Methyl-hydrocotoin
(Cotoin dimethyl ether)—$C_6H_5.CO.C_6H_2(O.CH_3)_3$. Melting point, 113° C.

These are all methyl ethers of a substituted benzophenone, or better, of benzoyl-phloroglucin.

Protocotoin—$(CH_3O)_2HO.C_6H_2.CO.C_6H_3$ CH_2. Melting point, 141–2° C.

Methyl-protocotoin—$(CH_3O)_3.C_6H_2.CO.C_6H_3$ CH_2. Melting point, 134–5° C.

Protocotoin and methyl-protocotoin are derivatives of 1,3,5-trioxybenzoprotocatechone and are the methylene ethers of hydrocotoin and methyl-hydrocotoin.

Phenyl coumalin—$C_6H_5—C : CH.CH.$
$\quad\quad\quad

ANALYSIS.

Ten grams of the bark were placed in an extraction thimble and extracted with light-boiling petroleum ether for about 20 hours. The solvent was then carefully evaporated, the residue dried in a desiccator and weighed at frequent intervals until the weight losses became constant. It was then heated at 110° C. to constant weight, with the following results:

Total petroleum ether extract	12.69%
Ethereal oil	1.89%

The thimble from the petroleum ether extract was dried and extracted with U. S. P. ether until exhausted.

Ether extract (after petroleum ether extraction)	10.25%

The thimble was again dried and extracted with 95% alcohol until exhausted.

Alcohol extract (after petroleum ether and ether extraction)	8.02%

The petroleum ether extract contained most of the cotoin. The alcohol extract contained tannin and alkaloid.

Ash	1.67%

Alkaloids.—Ten grams of the bark were placed in a 250-cc bottle and 200 cc of ether-chloroform mixture (2–1) added and thoroughly shaken, then made alkaline with ammonia and shaken at intervals, then allowed to stand over night. One hundred and seventy-five cc of the clear supernatant liquid were then drawn off into a cylinder and filtered, washing both cylinder and filter paper with ether. The alkaloids were repeatedly extracted with 2 per cent sulphuric acid until 2 cc of the acid gave no turbidity with iodine solution. The acid solution was then made ammoniacal and extracted with several portions of chloroform until all the alkaloids had been removed, as shown by test. Each chloroform extract was washed successively in two separatory funnels, each containing 15 cc of $N/2$ sodium hydroxide. The chloroform solutions were washed in a third separatory funnel with 10 cc of water and finally filtered into a tared flask. The chloroform was evaporated and the flask with contents dried to constant weight at 100° C. The alkali wash waters, containing any phenolic alkaloids, were added to the water in the third separatory funnel and acidified with hydrochloric acid. The alkaloidal acid solution was then made alkaline with ammonia and extracted with chloroform and treated as above. This method yielded two alkaloids or groups of alkaloids, one non-phenolic and the other phenolic as follows:

Total non-phenolic alkaloids	0.78%
Total phenolic alkaloids	0.60%
Total alkaloidal content of the drug	1.38%

At the suggestion of Dr. Rusby, the name *parostemine* is given to the non-phenolic alkaloid and *parosteminine* to the phenolic alkaloid. Both names are derived from *Parostema*, the sub-genus of Nectandra to which coto belongs.

Parostemine, the non-phenolic alkaloid, and *parosteminine*, the phenolic alkaloid, give no characteristic color reactions with the usual alkaloidal color reagents. Both precipitate with the usual alkaloidal precipitants. Parosteminine, being a phenol, as is shown by the fact that it is not extracted from a fixed alkali solution by chloroform, gives a purple-red color with ferric chloride in alcoholic solution. Mayer's reagent gives a well-crystallized precipitate with parostemine which in itself is characteristic since this is not the case with any of the common alkaloids. With parosteminine, the precipitate formed by Mayer's reagent is the usual curdy, amorphous mass. Wagner's reagent yields with parostemine a precipitate which rapidly becomes crystalline and sharply defined. Parosteminine withth is reagent forms a precipitate which remains amorphous and shows no tendency to assume a crystalline form such as is exhibited by parostemine.

Cotoin.—About 10 grams of the bark were extracted with 200 cc of ether, the ether evaporated to about 15 cc and then 100 cc of light-boiling petroleum ether were added in four portions, stirring thoroughly after each addition. The mixture was then brought to the boiling point and again stirred, filtered and the sol-

vent evaporated. The residue was dissolved in boiling water and crystallized. The slightly yellow crystals so obtained melted at 127–128° C. uncorrected. The alcoholic solution gave a brown-black coloration with ferric chloride. A few crystals dissolved in glacial acetic acid, on the addition of a few drops of concentrated nitric acid, gave a blood-red color. These reactions prove that the crystalline substance is cotoin.

SUMMARY.

Nectandra Coto Rusby is a true coto, since it contains cotoin. The total ether extract is 24.83%, volatile oil 1.89%, and ash 1.67%. Two new alkaloids, parostemine and parosteminine, were found in the drug. Further work is in progress and will be reported later in the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

RESEARCH LABORATORIES,
SEIL, PUTT & RUSBY, INC.,
NEW YORK.

THE HISTOLOGY OF VILCA BARK.

BY FANCHON HART.

Piptadenia macrocarpa Bentham is the botanical source of Vilca bark, one of the many medicinal barks brought here from South America by Dr. H. H. Rusby. This bark was collected by him during his recent exploration in the Amazon region.

The tree is a member of the family *Mimosaceae*. It was found growing in Bolivia where the natives make an aqueous extract of the bark. This extract is added to cane juice to hasten fermentation, the process being brought to completion in much less time than is otherwise required and resulting in an increased yield.

The tree has a wide range in central South America. Dr. Rusby encountered it on the central slopes of the eastern Bolivian Andes, at an elevation of from 3000 to 5000 feet, where the trees are abundant, growing on the slopes, but not in the river bottoms. The usual height of the trees is from 40 to 80 feet, and the trunk diameter from one to two feet. The tree is instantly recognized by its conspicuously warty bark, the warts so densely placed as to be freely confluent or superposed. The leaves are bipinnate, with innumerable very small leaflets, imparting a fine and graceful appearance to the foliage. The flowers are of the usual mimosaceous type and the pods like narrow flattened bean pods, with strongly thickened margins, brown in color and of a woody texture. The wood is extremely hard and very durable, and largely used as lumber.

It is noteworthy that this is one of the several trees of tropical America to which the name "quebracho" has been applied, so that there has been some confusion of it with the quebrachos of Argentina and Paraguay. It has also been called "Zumaque," doubtless because of its large content of tannin, showing a confusion with the several plants known in different regions as "sumac."

The bark is easily collected, peeling readily from the wood, and has been used for tanning, as well as for the fermentation of cane juice.

GROSS DESCRIPTION.

Older pieces of the bark dry in the form of large curved, warty, roughly scabrous quills, 50 to 60 millimeters in width and averaging 200 millimeters in length. The middle and inner bark is from 5 to 8 millimeters in thickness, the warts from 2 to 25 millimeters in thickness. *The outer bark* which is thickly covered with warty projections is rough and scaly. These warts are built up layer upon layer and are

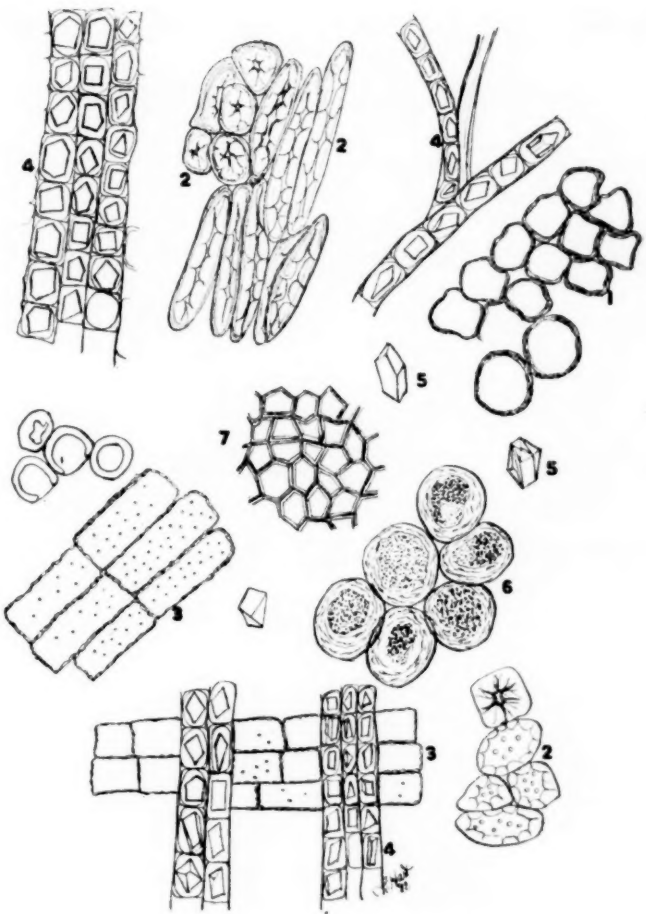

FIG. 1.—THE CELLULAR ELEMENTS AND CONTENTS OF VILCA BARK.
1—Cortical parenchyma; 2—Stone cells; 3—Medullary ray cells; 4—Crystal-bearing fibers; 5—Prismatic crystals; 6—Resin cells; 7—Bark parenchyma.

from 2 to 30 millimeters in diameter at the base. They are broadly conical or oblong in shape, deeply furrowed and concentrically striated. Externally they are gray to greenish brown in color, internally they are brownish yellow. *The middle bark* is pink to pinkish buff in color and breaks with a hard splintery fracture. After fracturing, the middle bark separates (with difficulty) into six to eight layers. *The inner bark* is red to brownish red in color, smooth to the touch and

marked with many fine longitudinal striations. Elevations which appear on the inner bark are caused by the protrusion of the tissues of the larger warts.

HISTOLOGICAL DESCRIPTION.

A cross-section of the bark (Fig. 3) through one of the warty projections shows the periderm to consist of many layers of cork tissue. Each wart is completely bounded by cork and contains bands of cork tissue together with some cortical parenchyma and many resin cells. Large lenticels and secretion cavities are apparent in the bark periderm. The cortical parenchyma of the middle bark contains many

FIG. 2.—THE CELLULAR ELEMENTS AND CONTENTS OF WARTY PIECES.

1—Cork cells; 2—Stone cells; 3—Porous bark parenchyma; 4—Resin cells; 5—Stone cells; 6—Bark parenchyma; 7—Prismatic crystals; 8—Resin masses; 9—Siliceous materials.

prismatic crystals. Bast fibers and porous striated stone cells are likewise found in this region. The inner bark consists of bast fibers, bark parenchyma and medullary rays. The above elements are shown in Fig. 3, cross-section of the bark.

The powdered bark, excluding the warty material, shows many large crystal-bearing fibers, composed of crystal cells. Large prismatic crystals fill the cavities

of the crystal cells, the walls of which are thickened at the corners. Porous and striated stone cells are seen in long and cross-section view. Masses of irregular cortical parenchyma cells and five- to six-angled yellow and reddish brown cells of the bark parenchyma are easily distinguished.

Medullary rays crossed by crystal-bearing fibers are seen in the form of broken fragments. Many circular red and yellow resin masses present a spongy appearance. Prismatic crystals are found free in the field.

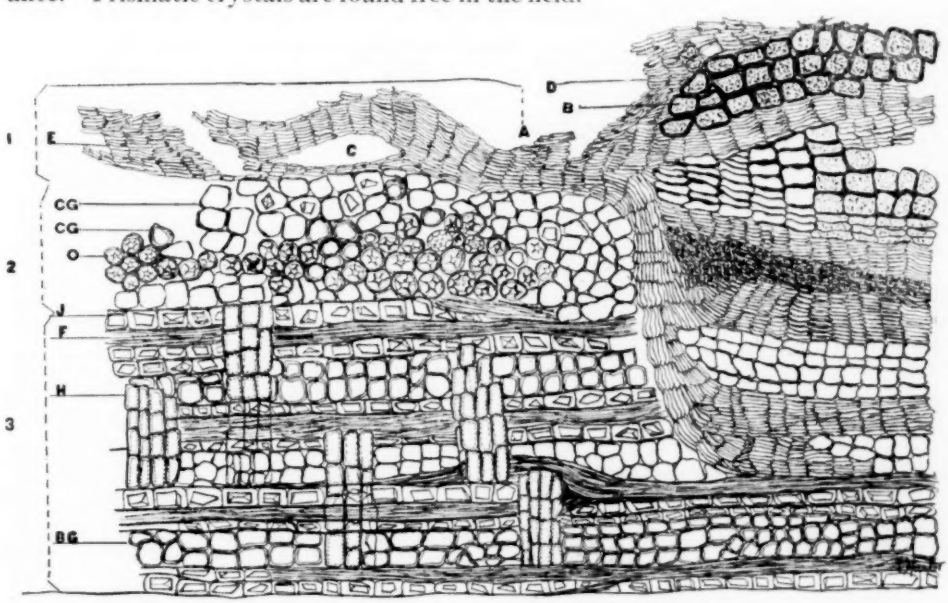

FIG. 3.—CROSS-SECTION OF VILCA BARK.

1—Outer bark: A, Lenticel; B, Thickened walled cork with tannin; C, Secretion cavity; D, Cork tissue; E, Periderm.
2—Middle bark: CG, Cortical parenchyma; F, Fibers; O, Stone cells; J, Crystal-bearing fibers.
3—Inner bark: F, Fibers; H, Medullary rays: BG, Bark parenchyma.

The powder prepared from the warty projections shows them to consist largely of cork and resin cells. Prismatic crystals, stone cells, cortical and bark parenchyma are found in smaller amounts than in the bark proper. Irregular pieces of siliceous material are present in considerable quantity.

The bark contains a large percentage of tannin, calcium oxalate and resin.

BOTANICAL DRUG RESOURCES OF NEW ENGLAND.

BY E. E. STANFORD.

The New England States furnish a considerable number of native plants which were largely collected for medicinal use in the colonial and early national periods but which now rarely enter commerce from this source. Many are no longer extensively used in commercial or prescriptive medicine, and those which are in demand can usually be more cheaply supplied by Southern Appalachian regions.

Increases in price and an influx of cheaper foreign labor into the rural districts suggest the possibility of commercializing at least some products. *Veratrum viride* and *Aspidium marginale* are examples of such materials. Drug cultivation appears scarcely to have been attempted here, though agricultural conditions suggest worth-while possibilities for a few products.

APPARATUS FOR CONTINUOUS PRECIPITATION BY COOLING.*†

BY M. R. MILLER.

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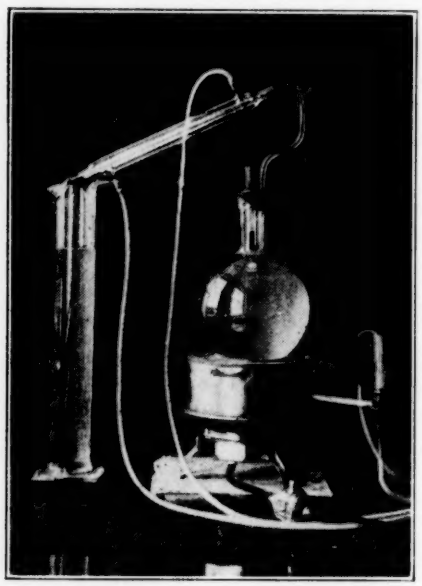
A number of operations, particularly in the preparation of organic compounds, call for solution of a crude material in hot solvent and the recovery of a more pure substance by cooling the hot solution. The process depends obviously on the difference in solubility of the substance sought at different temperatures. An arrangement of apparatus according to the following description and illustration makes this process a continuous one.



Apparatus for Continuous Precipitation.

The material to be extracted, usually a mass of crude product, is placed in the large flask with sufficient solvent to fill the flask. This is set on a hot plate or water-bath whereby the temperature of the solvent is kept just below the boiling point.

Through the stopper there pass three tubes, one, which is the leg of a siphon, extending nearly to the bottom of the flask: this provides for the return of the solvent to the flask after depositing its dissolved material in the cooling vessel. The second tube, which is the leg of a second siphon, extends to just below the surface of the liquid: this provides for the outflow of hot concentrated solution to the cooling vessel. The third tube is a short one by means of which the siphons are filled by pressure or suction when the apparatus is ready to start working. To this tube may be attached, if necessary, a reflux condenser to prevent the loss of solvent through the escape of vapor.

The cooling vessel in the illustration consists of a liter graduate but a liter flask or other deep vessel may be used. It is so set that when filled the surface of the liquid in it is level with that in the flask and is best placed in a cooling bath of water from the tap or a cooling mixture. Such a bath is not shown in the illustration.

The opposite leg of the first siphon is only long enough to extend barely below the surface of the liquid in the cooling vessel. By means of this siphon the cooled liquid returns from the cooling vessel into the flask or extracting vessel. The opposite leg of the second siphon extends two or three inches below that of the first and through this siphon comes the hot concentrated solution from the flask. This second siphon also forms the tube of a condenser, which is inclined somewhat

* From the Department of Research Chemistry, Nevada Agricultural Experiment Station, Reno.

† Published with the permission of the Director of the Nevada Agricultural Experiment Station.

and whose short jacket is supplied with water from the tap. The function of the condenser or cooler is to promote circulation by increasing the specific gravity of the solution.

When properly set up the hot concentrated solution flows through the siphon with the condenser, from the flask to the cooling vessel where precipitation takes place through cooling. The precipitated material falls to the bottom of the cooling vessel where it collects until removed. It was found that the gentle current set up through the action of the two siphons would carry but very little of the solid material back to the flask. By means of the apparatus the solvent dissolves the crude material, or the desired substance from it, deposits it on being cooled and returns to the flask for a further quantity—the advantages being continuous operation, requiring no attention, and economy of solvent.

This apparatus has served well in the writer's laboratory in the purification of saponin from the dried crude plant extract by precipitation from hot alcohol by the Schrader method.

ASSAY OF DIGITALIS BY INTRAMUSCULAR INJECTION IN THE FROG.

BY M. S. DOOLEY AND C. D. HIGLEY.*

There is no satisfactory method for the standardization of the digitalis bodies in spite of the extensive efforts that have been made to find one. The present paper describes a method which presents advantages over the procedures now followed.

Observers have criticized the present official method mainly on account of lack of uniform absorption from the lymph sac. It is toward the obviation of this particular difficulty that our experiments have been directed. This lack of uniform absorption is not merely inconvenient, but it interferes with the reliability of the method. This is indicated by the fact that more than twenty different methods have been proposed since Famulener and Lyon published the one-hour method in 1902.[1] In the search for a better method investigators have covered a wide field—chemical as well as biological—but, with the exception of the cat method, none has attracted much more than passing notice.

In common with other observers we have long recognized great variability in the results obtained in routine assays by the lymph sac method, especially when the attempt was made to utilize it in research. This may be illustrated by an experience of one of us (D.) while working in Dr. Hatcher's laboratory in the summer of 1920 (the season is here referred to because the variabilities appear to be greater at this time). The problem under consideration was the question of the rate of elimination of digitalis substances—a problem in which it was desirable to know the potency of a given specimen in advance of attempting the study of its rate of elimination. Poor absorption from the lymph sac rendered the one-hour method useless for this purpose and the twenty-four-hour toxic method was finally substituted.

I. ORIGIN OF THE PROBLEM AND DESCRIPTION OF THE METHOD.

During the course of the above experiments upon the elimination of digitalis substances mention was made of the feasibility of making injections into the

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abdominal vein of the frog which led to an attempt to develop a method of assay of digitalis bodies by means of intravenous injections in the frog. The results of these intravenous injections proved disappointing but in the course of experiments the idea of an intramuscular method suggested itself. Only a few trials were required to demonstrate its apparent superiority over the official method.

The method of preparing the drugs for this study was, for the most part, as follows: In the case of alcoholic preparations, tinctures and fluidextracts, an amount equivalent to the percentage of alcohol contained was evaporated off, in most instances spontaneously, but in some cases by slight heat (not above 50° C.) over a water-bath. Enough alcohol was then added to the residue to make the final product contain 15%, when 0.7% sodium chloride solution was added sufficient to make it up to the original volume. The largest total amount of fluid injected into any animal in our whole series, with the exception of two experiments with digitalin in which doses of 0.5 and 0.51 cc were injected, was 0.47 cc and this was in the case of a very large frog. In general the total dose averaged much less than these figures. The fluid dose per gram of frog was, with a few exceptions, well below the allowable 0.015 cc specified by the Pharmacopoeia. In one series of six animals receiving digitalin the per gram dose was from 0.016 to 0.021 cc but in the cases tinctures and fluidextracts of digitalis no per gram dose was larger than 0.01 cc. In some instances preparations have shown such high potency as to require dilution for the sake of accuracy but none have required concentration. This was done with 0.7% sodium chloride solution and enough alcohol to make the final product contain 15%. In the case of ouabain a 1 to 10,000 solution in 0.7% sodium chloride was always used. Digitalin was made up in 0.7% sodium chloride containing 15% alcohol. Where precipitates occurred, as was always the case with tinctures and fluidextracts, these were dealt with as directed by the Pharmacopoeia—the sample was always thoroughly shaken before a dose was taken out for injection. These sediments were never very abundant or so coarse as to clog the fine needles (26 and 27 guage) used for the injections. A tuberculin syringe was used to measure the total dose and the injections made directly from it.

The procedure for intramuscular injections is simple and may be briefly described as follows: The frog is held with its back against the palm as in the official method, but with the head downward. The edge of the palm and the little finger fit in back of the fore legs and offer resistance to the pull on the hind legs being held, one between the thumb and fore finger, the other between the middle and ring fingers. In this way the hind legs are grasped below the knees and spread apart, care being taken not to stretch the skin over the thighs. The finest needle (27 guage) is used and half the total dose is injected slantingly into the thickest part of each thigh. A little experience taught us to avoid the large vessels as certain negative results could be attributed to hemorrhage.

In a preliminary report[2] the results of studies of ouabain and some preparations of digitalis have already been summarized in which it was shown that the required S. S. S. (systolic standstill) dose was always smaller, and the end-point sharper, than is true when equivalent doses are injected into the lymph sac. Additional data are now presented, much of which is even more conclusive than that originally published.

TABLE 1.

Frogs.	Drug No.	S. S. S. Dose in Mg./Gm. Lymph sac.	Intramuscular.	Percent.
		Crystalline Strophanthin (Ouabain).		
Lot 1	1	0.00045	0.00037	17.8
Lot 2	1	0.00051	0.00044	13.8
Lot 3	1	0.00032	0.00027	15.7
Lot 4	1	0.00039	0.00031	20.6
Lot 5	2	0.00059	0.00050	15.3
Lot 6	2	0.00057	0.00051	10.6
		Digitalis—Tinctures.		
Lot 1	1	0.70	0.57	18.6
Lot 2	2	0.59	0.49	17.0
Lot 3	3	0.72	0.55	23.6
Lot 3	4	1.03	0.72	30.0
		Digitalis—Fluidextracts.		
Lot 1	1	0.90 Neg.	0.70	22.3
Lot 2	2	0.60	0.50	16.7
Lot 3	3	0.58	0.49	15.6
Lot 3	4	0.92	0.60	34.7
Lot 3	5	0.64	0.56	12.5 (24 hr.)
		Digitalin—Merck. *Formerly known as "German."*		
Lot 1	1	0.025	0.022	12.0

Table 1 summarizes the results. It contains the condensed result of all experiments with ouabain, digitalin, tinctures and fluidextracts of digitalis. In all cases the intramuscular has been compared with the S. S. S. dose by lymph sac and has always been found smaller. The last column of the table shows the percent difference between the two in corresponding lots of frogs. The effective intramuscular dose of digitalin is seen to be 12% less (single series), while with tinctures and fluidextracts the differences average, respectively, 22 and 22.2%. With ouabain the difference lies intermediate—15% (approximately). It may be noted in passing that digitalin was one of the most difficult of our series to assay. It seems advisable, also, to call attention to the rather wide variations in the percent column for the digitalis preparations. The high values were derived from experiments during the summer season. Other observers have reported poorer absorption from the lymph sac during the summer and that has always been our experience. It is believed, therefore, as the other figures in the table show, that the differences will not average as great during the other seasons of the year.

DISCUSSION.

It is apparent from the above tabulations that the drugs under consideration develop a more intensive effect by from 10 to approximately 35% within the hour, injected intramuscularly, than when acting from the lymph sac. When one attempts to explain this discrepancy difficulties arise. One cause already cited—incomplete absorption from the lymph sac—is evident enough in some experiments, but by no means in all (see discussion of ouabain, next pages). The presence of fluid in the lymph sac at the end of an experiment is commonly set down as evidence of this but, of course, may or may not be correct, for, while it is usually associated

with a negative result, this is not a fixed rule. The fluid remaining may contain only a negligible fraction of active principle. In the case of intramuscular injections inspection of the regions of injections and the constancy of results indicate uniform absorption in nearly all cases, but other objective proof is desirable if it could be had. Intravenous injections would not serve as controls. The twelve- and twenty-four-hour toxic methods yield values far higher, hence, if completeness of absorption is to be judged solely by the size of the minimum dose required, this would indicate that absorption is far more complete by the intramuscular route. But, as complete absorption occurs in many of the animals in the twenty-four-hour experiments that have not died but which have received doses greatly in excess of those giving positive results in the one-hour intramuscular experiments, it is evident that there is at least one and, we believe, more than one other factor influencing the final result in a given case. These are the rates of absorption and elimination. As indicated below a distinction should be made between rate of and completeness of absorption, in relation to the time limits set for the experiments, although one of these factors is dependent upon the other. In going over our notes it is found that, in a number of instances in which animals have received equivalent dosage and in which complete absorption has been noted, the results have been partly negative, partly positive. How are such to be explained? The usual practice has been to dismiss the question by the stock expression that some of the animals are more susceptible than others. But this empiric explanation does not explain. Is it not more likely that variation in the rate of absorption has made the difference? Rather, it may be more correct to say that the final result will be conditioned upon the relative rates of absorption and elimination. If it is assumed that two animals are given the minimum effective dose, the one will absorb the total dose, let us say, in 35 minutes, whereas the other just completes the process by the end of the hour, is it not probable that systolic standstill will occur in one case and not in the other? It is evident that such difference in susceptibility is a matter of how promptly an effective concentration is built up in the circulation. It must be apparent that some such mechanism is back of the greater susceptibility from intramuscular injections. More especially is this the case when ouabain is used, for the protocols show that complete absorption occurred in almost every one of our numerous experiments in which it was used by both methods. It is believed, therefore, that the results warrant special emphasis upon this point, particularly as there is strong probability that most of the digitalis substances begin to be eliminated at variable rates as soon as they reach the circulation.

Hatcher has shown that, in some types of mammals, most of the digitalis substances begin to disappear from the circulation promptly on entering it but at different rates, compared one with another, and at different rates in different species of animals.[3] One of us (D.) has shown that the size of the minimum lethal dose for the cat, by vein, is governed materially by the rate of injection.[4] In the case of slow injections the minimum lethal dose was found to be much larger than where the dose was allowed to enter the vein at a fairly rapid rate. In the former case elimination was going on and had to be made good by further injection. As applied to the present problem any delay in absorption from the lymph sac or muscles would similarly influence the necessary dose. It is evident,

therefore, that the more adequately the rate of entrance into the circulation keeps pace with the rate of elimination the smaller will be the required dose for a given effect.

It is not a pure assumption that elimination goes on at a fairly rapid rate in the frog, for it has been observed repeatedly that if animals in which the ventricle is almost in systolic standstill at the end of the hour be kept under observation for a time, their hearts will resume rhythmical beating. We venture the suggestion that if any worker who assays by the official method would keep his animals under observation for a longer period than required by this method, some of the hearts recorded as positive would, in time, resume rhythmic activity. This is taken to mean that elimination has, meantime, lowered the concentration of the drug necessary to hold the heart in systole.

The following experiment may be cited as a more direct proof of the fact that most of the active digitalis substances are rapidly eliminated by the frog. By the device of injecting the dose in four or five equal parts into different regions of the muscles at half-hour intervals instead of injecting the whole amount at once and

TABLE 2.

Tabulation to Show Relative Constancy of Effects with Lymph Sac and Intramuscular Injections.

Ouabain.							
Lymph Sac—Mg./Gm. Body Wt.			*Abs.*	*Intramuscular—Mg./Gm. Body Wt.*			*Abs.*
0.0005–0.00055	S. S. S.	tend. beats	C	0.00047–0.00049	S. S. S.	tend. s. b.[1]	C
0.00056	S. S. S.	+	C	0.00049	S. S. S.	+	C
0.00057 (2 expts.)	S. S. S.	tend. s. b.[1]	C	0.0005 (3 expts.)	S. S. S.	+	C
0.00058 (2 expts.)	S. S. S.	+?	C	0.00051 (2 expts.)	S. S. S.	tend. s. b.[1]	C
0.00058	S. S. S.	+	C	0.00051	S. S. S.	+	C
0.00059	S. S. S.	tend. s. b.[1]	C	0.00052–0.0006	S. S. S.	+	C
0.00059	S. S. S.	tend irreg. b.	C				
0.00059	S. S. S.	+	C				
0.0006	S. S. S.	+	C				
0.0006	S. S. S.	+?	C				
0.00065	S. S. S.	+	C				

[1] s. b. = Slow beat.

then examining the animals at the end of two and a half or three hours it was found that a 25 to 30% larger dose was required. It is assumed that this 25 to 30% difference represents the amount the animal has eliminated during the longer interval of the experiment over that of the one-hour period with which it is compared.

Tables 2 and 3 show the contrast between the results afforded by the two methods that are discussed in this paper. They are inserted to illustrate the difference in sharpness of end-point. Table 2 is typical of the results obtained with ouabain by the two methods on the same lot of frogs. It will be noted that in the case of the intramuscular injections the results tend to be negative up to a certain intensity of dosage—in this experiment, 0.0005 mg. per Gm. of frog—and all dosages to be positive above that level, whereas, in the case of injections into the lymph sac, negative results are interspersed with positive over a wide range of dosage. With any of the preparations of digitalis the differences are usually more marked, as shown in Table 3. Tinctures and fluidextracts show the greatest difference,

TABLE 3.

Tabulation to Show Relative Constancy of Effects from Lymph Sac and Intramuscular Injections. Some of the Higher and Lower Dosages, Not Significant, Have Been Left Out of This Summary. It May Be Seen That If, under the Intramuscular Column, the Second 0.51 in Which a Hemorrhage Was Noted Is Excluded, There Is a Satisfactory Line of Demarcation between Positive and Negative Values. Under Lymph Sac Column the Not Unusual Ragged End-point Is in Evidence.

	Digitalis—Tincture.		
Lymph Sac—Mg./Gm. Body Wt.	*Abs.*	*Intramuscular—Mg./Gm. Body Wt.*	*Abs.*
0.49 S. S. S. tend. b. s.[1]	C	0.48 S. S. S. tend. b. s.[1]	C
0.50 S. S. S. +	C	0.49 S. S. S. +	C
0.50 S. S. S. tend. b. s.[1]	C	0.49 S. S. S. +	C
0.51 S. S. S. tend. b. s.[1]	C	0.50 S. S. S. tend. b. s.[1]	C
0.52 S. S. S. tend. b. s.[1]	C	0.50 S. S. S. +	C
0.53 S. S. S. +	C	0.50 S. S. S. +	C
0.54–0.58 S. S. S. nearly	Inc.	0.51 S. S. S. +	C
0.59 S. S. S. +	C	0.51 S. S. S. tend. hemorrhage	
0.60 S. S. S. +	C	0.52 S. S. S. +	C
0.60 S. S. S. ?	C	0.53 S. S. S. +	C
0.60 S. S. S. ?	C	0.53 S. S. S. +	C
0.61 S. S. S. tend.	C	0.53 S. S. S. + hemorrhage	C
0.61 S. S. S. nearly	Inc.	Absorption complete in this	
0.62 S. S. S. nearly	C	series so far as autopsy could show.	
0.63 S. S. S. +	C		
0.64 S. S. S. nearly	C		
0.65 S. S. S. tend. irreg.	C		
0.70 S. S. S. tend. b. s.[1]	C		
0.75 S. S. S. +	C		

[1] b. s. = Beats on stimulation.

just as they also show the greatest disparity in the S. S. S. dose, by the two methods. This combination of excessive dosage required by the official method and the uncertainty of end-point robs an assay of most of its value, and results furthermore in additional expense and much loss of time.

It has been suggested that frogs obtained from different localities may show differences in their capacities for absorption of the different digitalis bodies. This seemed to us to be worthy of investigation, for if such differences really exist the Pharmacopoeia should at least specify the region from which the frogs are to be taken.

As a matter of fact we have not observed any such differences dependent upon the source of supply. Frogs caught recently in the region about Syracuse behaved in this respect much like those obtained from Chicago. It appears to us, on the other hand, that the fundamental difficulty lies with the lymph sac as an absorbing mechanism for it may be here noted again that, even with a readily absorbable material like ouabain, an average of over 15% (see Table 1), or more than one-sixth of the total dose, is held back from absorption within the hour. It can be seen that even greater differences in absorption from the lymph sac will be observed when one uses different galenical preparations of digitalis made by different methods employed by different manufacturers. This can hardly fail to have a practical bearing on the problem of manufacturing standard preparations.

Most of the samples used in this research have it stated on the labels that they have been prepared by the official method, from assayed leaves. The inference

is drawn that assay has been by the official method but when an assay has been attempted by the same method utter failure has resulted in some cases and in others lack of a sharp end-point (see Table 3). We are prompted to ask how the manufacturer definitely accomplishes an assay when, in our experiments, most of the doses were found, in large part, in the lymph sac at the end of the hour.

That the rapidity of absorption plays an important rôle in the effects under consideration is still further evidenced by some recent experiments performed with strychnine. Exactly the same procedures have been carried out as with digitalis, except the adoption, as an end-point in this instance, of the interval required after the drug is injected for a convulsion to develop. Two main points have been developed. First, convulsions develop much sooner—our data are too meager to enable us to say how much sooner but in some cases, 100%—after intramuscular injections. Second, the minimum intramuscular convulsive dose will not induce convulsions acting from the lymph sac.

There are three factors that must be considered with reference to absorption from the muscle. In the first place it is well known that the muscles have an abundant blood supply. In the second place the animals are usually somewhat active following the injection, their movements serving to massage the area of injection, thus favoring the wider distribution of the drug and bringing it into contact with a larger surface, thereby promoting absorption. This could not happen in the case of the lymph sac. In the third place the injection of the dose in two parts in different areas serves this end also.

SUMMARY.

1. The need for a modification of the present Pharmacopoeial method of digitalis assay to insure more uniform absorption is pointed out.

2. A method involving the intramuscular injection in the frog is described. It is simpler and gives more nearly uniform results.

3. Data are presented to show that the dose is smaller and the end-point sharper than in corresponding injections into the lymph sac.

4. The more rapid and complete absorption plays a dominant rôle in developing greater toxicity from intramuscular injections.

5. The probability that the rate of elimination of drugs in the frog, as in mammals, plays an important rôle in the final result is discussed.

6. It is believed that the great variability of many presumably assayed commercial preparations is due to reliance having been placed in the method of injection into the lymph sac.

7. The better absorption from the muscles is due to division of the dose, better blood supply, and movements of the animals.

LITERATURE.

No attempt is made to review the literature on the development of methods for the assay of digitalis as an admirable summary down to 1916 is to be found in the following bulletins from the Hygienic Laboratory, Washington, D. C.:

(*a*) Edmunds and Hale, *Bulletin* 48, 1908.

(*b*) Hale, *Bulletin* 74, 1911.

(*c*) Roth, *Bulletin* 102, 1916.

One other contribution since that time may be noted:

(*a*) Knudson and Dresbach, *Proc. Soc. Exp. Biol. and Med.*, 19, No. 8, 1922.

(*b*) Knudson and Dresbach, *Jour. Phar. and Exp. Therap.*, Vol. 19, 1922.

1. Famulener and Lyon, PROC. AM. PHARM. ASSOCIATION, 50, 415, 1902.
2. Dooley and Higley, *Soc. Exp. Biol. and Med.*, 19, 250, 1922.
3. Hatcher, *Arch. Int. Med.*, 10, 169.
4. Dooley, *Jour. Phar. and Exp. Therap.*, 17, 277, 1921.

DETERIORATION OF THE TINCTURE OF DIGITALIS.*

BY CHAS. C. HASKELL, D. S. DANIEL, AND G. S. TERRY.

The keeping qualities of the tincture of digitalis has been the subject of many investigations. In one of the earliest papers reporting the results of such a study, Houghton and Hamilton[9] concluded that there was a loss in the strength of the tincture with age. Two years later, Sharp and Lancaster and Sharp and Branson[16,17] presented evidence indicating that there was a definite loss in the activity of certain tinctures, becoming manifest at the expiration of 15 months. Goodall,[3] from the examination of 23 samples, arrived at about the same conclusions as those reached by the authors just mentioned. According to his assays, there was no loss in strength up to 14 months; but, after this, some of the samples showed a decrease in potency; and, at the end of 3 years, one tincture possessed less than one-third of its original toxicity. He cites Hanes as saying that the tincture keeps for two years without material change in activity, while Moran makes the claim that there is no important amount of deterioration up to 3 years. From assays on a number of liquid preparations of digitalis, Hale[4] concluded that the rate of deterioration differed in different cases, but that some occurred with age in all of his samples. O'Brien and Snyder[11] observed a rapid loss in the activity of a tincture, originally of a very high degree of potency, this loss amounting to 55% in the course of $2^1/_2$ years. Even more remarkable rate of deterioration was reported by Schmidt and Heyl[15]—a tincture tested by them being found to have retained only 40% of its original strength at the end of 15 months. Indeed, all of the preparations examined by Schmidt and Heyl lost strength so rapidly that one is led to suspect that the conditions under which their experiments were carried out differed from the ordinary.

All of the investigators who have been cited employed one of the various frog methods in testing the specimens examined. While their conclusions as to the rate of deterioration are far from being in complete harmony, their results do agree in indicating that the tincture of digitalis loses strength in relatively short periods of time, when judged by the criterion of the frog test. From the meager reports of similar experiments carried out on guinea pigs, the same inference may be drawn. Employing the guinea-pig method, Pittenger and Mulford[14] reported a rate of deterioration surpassing even the unique observation of Schmidt and Heyl; for, after 7 months, a tincture tested by them retained little more than a quarter of its original toxicity. Only one of the specimens which Pittenger and Mulford examined failed to show deterioration; and they state ". . . that, in most cases, tincture of digitalis not only deteriorates, but deteriorates very rapidly." As Hamilton remarks,[5] the acceptance of such "revolutionary" conclusions as these is tantamount to holding that the tincture of digitalis is a useless preparation;

* Scientific Section, A. Ph. A., Cleveland meeting, 1922.

its strength, "in most cases," having been so reduced before the patient receives it that therapeutic results can scarcely be hoped for. It is well recognized that the guinea-pig method is accompanied by important sources of error, and it is at least possible that some of these were overlooked by the Philadelphia investigators. Indeed, in a later paper, Pittenger[13] seems to take a more optimistic view as to the keeping qualities of the tincture of digitalis, for he reports a maximum loss of activity amounting to 46% in 12 months, as compared with the former report of almost 75% in 7 months. Even though more experimentation and further reflection may cause a still greater modification of the views held as to the stability of the tincture of digitalis, as judged by the guinea-pig method of assay, it seems justifiable to assume that this method, as well as the frog methods, indicates a definite loss in activity of the tincture in time.

Opposed to the results obtained on frogs and guinea pigs are the findings of Hatcher and Eggleston,[7] when Hatcher's cat method of assay was employed. From numerous experiments on cats, these authors were convinced that deterioration of liquid preparations of digitalis containing 50% or more of alcohol did not occur to any extent worthy of consideration in reasonable lengths of time. The criticism has been offered[14] that these conclusions were based on a single assay of old preparations, the initial strength of which was unknown. The following quotation shows that this criticism in unfounded: "We began by making new tests of the activity of our own old samples of the leaf and of tinctures made therefrom. *Comparing the results of these tests with the records of the previous ones, we found that none of the specimens which were four or five years old showed any material deterioration.*" (Italics ours.)

In the investigation by O'Brien and Snyder[11] previously referred to, a tincture and fluidextract of digitalis were assayed by the cat method and the assay repeated at the end of $2^1/_2$ years. So far as can be gathered from their protocols, these authors used a single cat for each of the initial assays and one or two for each of the subsequent ones. From the results of these tests it was concluded that, judged by its toxicity for cats, the tincture had lost about 30% of its strength in the lapse of time mentioned. While their figures check remarkably well, it would seem unsafe to base conclusions as to the strength of a digitalis preparation on a determination of its toxicity for one or even two cats; especially, when these conclusions are so opposed to those drawn by the two men most experienced in the use of the cat method. It was felt that further study would be of interest, not only as regards the rate of deterioration as determined by the cat method, but, possibly, also by shedding some light on the relative value of the cat and frog methods as means of determining the therapeutic worth of digitalis preparations.

In the fall of 1916, the Department of Pharmacy of the Medical College of Virginia was furnished with twelve samples of digitalis leaf, grown in the vicinity of Richmond by Mr. J. W. Wilber. The plants were all of the first year's growth and all of the species *purpurea;* from the appearance of the leaf, however, they seemed to represent twelve distinct varieties. Tinctures were made from these samples, according to U. S. P. IX; but, unfortunately, we were not informed as to the manner of drying the leaf nor the exact date of percolation. (The digitalis was percolated some time during the months of November or December 1916.) Dur-

ing January, February, March, and April 1917 all of the samples were tested by the one-hour-frog method; nine by the cat method, and four by the guinea-pig method. By all three methods, an unusual degree of potency was shown; at present, however, we shall consider only the results obtained by the cat method.

In testing the samples on cats, we followed, in essentials, the directions of Hatcher and Brody.[6] Only adult animals were used; in a few instances, a lactating or pregnant female was included in a series, but only when the reaction of such an animal showed no marked deviation from the others used in the series. It has been our experience, in accord with that of Hatcher[6] and Morris,[10] that lactation or pregnancy may markedly influence the resistance of a cat to poisoning by digitalis, but this is by no means invariably the case. As a rule, ether was used for anesthesia; occasionally, chloretone, 0.2 gram per kilogram body weight, was administered orally or intraperitoneally. The tincture was diluted with either nine or nineteen parts of physiological saline, and the injections were made into the femoral vein from a burette. The extremes for the time consumed in the injections were 28 minutes and a little less than two hours; in most cases it averaged about 45 minutes. In the later tests, a rate of injection of 1 cc of the diluted tincture every $2^1/_2$ minutes was arbitrarily adopted, regardless of the strength of the sample or weight of the cat. This seemed justifiable, in view of the fact that the samples showed no extreme variations in strength and the weight of the cats employed in most of the tests was fairly uniform. In the original communication of Hatcher and Brody[6] it was stated that a sublethal dose of the tincture should first be injected intravenously and, after an interval of about fifteen minutes, a solution of ouabain should be slowly injected until the death of the animal occurred. In no instance did we use this "combined method;" the diluted tincture alone was slowly injected until death was produced.

After completion of the initial assays, the tinctures were kept in flint, cork-stoppered bottles, in a laboratory frequently unheated for considerable periods of time in the winter and unusually hot in summer, being directly under the roof. From time to time most, if not all, of the bottles were opened, and small amounts of the contents taken out, the frequency with which this was done varying in the different cases. Several of the samples were retested in 1921, but no systematic examination was undertaken until April, May, and June of the present year, when all nine of the samples were again assayed on cats. The results of the initial assays (1917) and the later assays (1922) when considered separately seemed satisfactory, but, when the figures of the different assays were taken together and subjected to critical analysis, it was evident that only those obtained for four of the samples could be relied upon. The unsatisfactory outcome of the assays of the other samples was due to imperfections of the method in our hands; in order to make these clear, a lengthy discussion of the cat method would be necessary. This we do not wish to enter into now.

TABLE I.—SUMMARY OF RESULTS OF CAT ASSAYS IN 1917 AND IN 1922.

No. of sample.	First assay in mg. per Kg.	Time lapse in months.	Second assay in mg. per Kg.	Percentage change.
9	55.7	64	62.5	−12.2
31	68.2	61	70.0	− 2.6
36	42.2	63	40.8	+ 3.3
39	71.2	64	64.0	+11.2

The figures for the assays of these four samples, both in 1917 and in 1922, are given in Table I.

It is evident from these figures that the four samples have undergone no appreciable change in the period of a little over five years. It has been claimed that the method permits the estimation of digitalis preparations with an error not greater than 10%; the changes indicated by the assays practically are within this limit. It would seem unlikely that of nine samples prepared from leaf of the same source and in exactly the same manner, four would prove stable and the remainder show deterioration when all were kept under the same conditions. Unfortunately, as has been mentioned, our results do not justify any conclusions in regard to the remaining five samples; they do show, however, that two closely checking cats do not prove the strength of a tincture of digitalis. This, of course, disproves the contention of O'Brien and Snyder[11] in regard to deterioration of their specimens, because their claim is based upon an entirely inadequate number of animals. On the whole, our results on all of the samples are in harmony with those of Hatcher and Eggleston,[7] and they have convinced us, at least, that tincture of digitalis shows no appreciable loss in activity in reasonable lengths of time, when judged by the criterion of the cat method of assay.

From the review of the literature bearing on the uses of a frog method in aging experiments, it seems fairly conclusively shown that tincture of digitalis loses strength in comparatively short periods of time as judged by this test. Accepting the view that the cat method fails to show deterioration of the tincture while the frog method does indicate such a change, what explanation is to be offered for the different results of the two methods? As is well known, absorption plays an important part in the frog and guinea-pig methods of assay, while in the cat method, since intravenous injection is employed, the question of absorption is eliminated. So far as we can ascertain, Hatcher and Eggleston[7] are the only ones who have remarked on this very obvious explanation for the difference in the results obtained by the different methods. According to these authors, Cloetta has stated that digitoxin is developed in the tincture of digitalis only on standing and, since digitoxin is irregularly and poorly absorbed from the lymph spaces of the frog, a conversion of some of the absorbable active constituents of the tincture into the poorly absorbable digitoxin would make it appear that the preparation had deteriorated when assayed by the frog method. A question of practical importance is whether a similar decrease in absorbability from the human gastro-intestinal tract also takes place in time. Digitalis is generally administered orally, and, if it is poorly absorbed, this is equivalent to a loss in strength, suggesting that the question of absorbability from the lymph sac of the frog, long considered a serious drawback to the method may, in fact, furnish us with important information which is not obtained when the cat method is employed. Attention has recently been called to the occurrence of tinctures apparently active when tested on the cat but unsatisfactory when employed clinically. The suggestion has been made that the failure to obtain therapeutic results with these preparations was due to a delay in or absence of absorption from the human alimentary tract. Though it has been assumed[12] that absorption from the lymph sac of the frog parallels that from the human intestine, this has not been proved; indeed, the investigations of Hatcher and Eggleston[2] incline to the opposite conclusion. Experiments which are in prog-

ress in this laboratory indicate that the change which occurs in the tincture of digitalis as the result of age does not interfere seriously with absorption from the alimentary tract of the cat.

CONCLUSIONS.

1. From the published results it seems clearly shown that the tincture of digitalis loses strength rather rapidly, as judged by the frog or guinea-pig method of assay.

2. With Hatcher's cat method, when sufficient numbers of cats are used to justify inferences, no apparent loss of strength in the tincture of digitalis can be detected in a period of as long as five years.

3. The difference in the results obtained by the two methods is probably explainable by the reference to a decrease in the absorbability of the tincture from the lymph sac of the frog.

4. Aging does not cause any marked decrease of absorbability of the tincture from the alimentary tract of the cat.

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MISCELLANEOUS CHEMICAL PAPERS.*

Absorption of Gases by Pinene.

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Kindt,[1] in 1802, obtained pinene hydrochloride by saturating well-cooled, dry pinene with dry hydrochloric acid gas. Subsequently, somewhat similar compounds were formed by the action of hydrobromic and hydriodic acids. By heating pinene with paraformaldehyde, resulting most likely in the dissociation to formaldehyde, Kriewitz[2] obtained an alcohol corresponding to the formula $C_{11}H_{18}O$. Various attempts have been made to combine hydrogen with pinene in order to study the reduction compounds. Pinene is reported[3] as forming no characteristic derivatives when treated with CO and CO_2. The absorption of oxygen by pinene, reported first by Kingzett,[4] has been well established as have also the resulting products formed therefrom. Papasogli,[5] in 1876, asserted that the oils (such as turpentine oil) absorb nitrogen as well as oxygen from the air, as did also Bardsky[6] in 1882. With the exception of the above the literature on pinene is practically devoid of any reference to the absorption of gases by that substance. Whereas the absorption of HCl, etc., has led to the formation of distinct chemical compounds, the absorption of so-called indifferent gases has thus far received little or no attention.

CARBON DIOXIDE.

In connection with the purification of pinene and the well-known oxygen absorption by this hydrocarbon with the changes subsequent thereto, the possibility that it might also absorb carbon dioxide suggested itself. Although *a priori* it did not seem probable that such absorption would take place to any appreciable extent or have any marked influence on the pinene, at all comparable to that produced by the absorbed oxygen, it seemed desirable to ascertain the facts whatever they might prove to be. Hence, a few experiments in this direction were made, more with the desire to satisfy the curiosity roused by the suggestion than with the expectation of the results which were obtained.

Thirty ccm. of pinene were transferred to the graduated tube of a Lunge nitrometer and supported by water. Carbon dioxide was then passed into the apparatus so that it came in contact only with the pinene. Whether the carbon dioxide was under slight pressure or not, its absorption was very noticeable. In 24 hours, all but 1.4 cc of 37.8 cc of gas, *viz.*, 36.4 cc CO_2, had been absorbed. The remaining gas was discharged and the apparatus recharged with an additional 30 cc of gas. After 24 hours all but 2.6 cc had been absorbed, *viz.*, 27.4 cc. The operation was repeated and after a third 24 hours all but 10 cc of 30 cc gas, *viz.*, 20 cc of CO_2, had been absorbed. In all 30 cc of pinene had absorbed 73.8 cc of CO_2 in three times 24 hours.

In the course of time the water column underlying the pinene became turbid as though the modified pinene had gone into partial solution. Tested with lime water, the aqueous layer gave a heavy precipitate. When previously boiled, no such precipitation occurred. This would seem to indicate that some of the carbon dioxide, first absorbed by the pinene, passed through the column of 30 ccm. of hydrocarbon and by it was given off to the water and that some of the modified pinene had gone with it.

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* From the laboratory of Edward Kremers.

A portion of the pinene was then shaken with lime water resulting in a copious precipitate. Another portion was boiled before being shaken with lime water, but this also gave a precipitate with the reagent. This would indicate that whatever the physical or chemical union between pinene and carbon dioxide, enough of the latter remains with the pinene after heating to 155°, the boiling point of pinene, to give the characteristic reaction with lime water reagent. Fresh pinene shaken with lime water gave not even a turbidity.

In order to ascertain something more about the nature of the carbon dioxide solution in pinene, 100 Gm. of freshly distilled hydrocarbon (b. p. 155–156°) were transferred to a shaking tube and CO_2 slowly forced into the tube for 48 hours. No increase in weight could be detected. However, the liquid had acquired a faint yellowish color, also a number of small, colorless granules had been formed. The following constants were ascertained: (1) for the rectified pinene; (2) for the hydrocarbon after it had been charged with CO_2; and (3) for the charged hydrocarbon after direct distillation. Fifty-five Gm. of charged hydrocarbon upon distillation yielded 0.1724 Gm. of gas, collected by passing it through potash bulbs, corresponding to 0.31 percent of the carbonated product.

	Before charging.	After charging.	After distillation.
Sp. gr. at 20°	0.860	0.862	0.861
α_D^{20} for 100-mm. tube	24.1°	24.1°	24.1°
n_D^{20}	1.4678	1.4681	1.4680
A. V.	0.56	0.54	0.54
S. V.	0.0	2.2	2.1
S. V. after acetylation	12.0	10.8	19.0

The changes in density and refractive index are just what one might expect. However, the differences are so small that it might not be an easy matter to duplicate the exact results. The angle of rotation apparently is not affected at all.

The acid values would seem to indicate that the presence of CO_2 had a negative effect, which does not seem correct. However, the differences are so small that they may be within experimental error. Of the chemical constants the saponification values are the most striking. Moreover, they seem to indicate that it is chemically combined and not merely physically dissolved carbon dioxide which affects this constant. The saponification values after acetylation reveal the greatest differences, but these differences are of such a nature as not to admit of rational interpretation, at least at present.

In order to secure data on the relative length of time for the CO_2 to penetrate the layer of pinene the following experiments were performed.

A Lunge nitrometer was filled with lime water, 30 ccm. of pinene were allowed to flow in from the top of the tube, and 30 ccm. of CO_2 forced in, atmospheric pressure being maintained in the nitrometer. The following results were recorded:

	I.	II.
First appearance of cloudiness in the lime water	10 minutes	9 minutes
CO_2 absorbed in that time	6 ccm.	5.2 ccm.
15 ccm. of CO_2 absorbed in	50 minutes	40 minutes

A third experiment was performed in like manner to the above, the results of which are as follows:

1	ccm. of	CO_2	absorbed	in	3	minutes	6	ccm. of	CO_2	absorbed	in	$12^1/_2$	minutes
2	"	"	"	"	5	"	7	"	"	"	"	$14^1/_2$	"
3	"	"	"	"	7	"	8	"	"	"	"	17	"
4	"	"	"	"	$8^3/_4$	"	9	"	"	"	"	$19^1/_2$	"
5	"	"	"	"	$11^1/_2$	"	10	"	"	"	"	22	"

The results are somewhat variable, being due, no doubt, to the presence of moisture in the upper portion of the tube.

For that reason a second series of experiments was run as follows: the nitrometer was thoroughly dried, 35 ccm. of pinene were placed in the bottom of nitrometer and forced up the tube by the lime water, thus preventing the upper portion of tube from becoming moistened by the lime water. The results obtained are as follows:

1	ccm.	CO_2	absorbed	in	2	minutes	0.3	ccm.	CO_2	absorbed	in	1	minute
2	"	"	"	"	$3^1/_2$	"	0.9	"	"	"	"	2	"
3	"	"	"	"	$5^1/_2$	"	1.6	"	"	"	"	3	"
4	"	"	"	"	7	"	2.1	"	"	"	"	4	"
5	"	"	"	"	9	"	2.7	"	"	"	"	5	"
6	"	"	"	"	11	"	3.4	"	"	"	"	6	"
7	"	"	"	"	13	"	4.0	"	"	"	"	7	"
8	"	"	"	"	15	"	4.6	"	"	"	"	8	"
9	"	"	"	"	17	"	5.1	"	"	"	"	9	"
10	"	"	"	"	19	"	5.6	"	"	"	"	10	"
11	"	"	"	"	22	"	7.0	"	"	"	"	13	"
12	"	"	"	"	$24^1/_2$	"	8.0	"	"	"	"	15	"
13	"	"	"	"	$27^1/_2$	"	10.0	"	"	"	"	20	"
14	"	"	"	"	$30^1/_2$	"	11	"	"	"	"	$22^1/_2$	"
15	"	"	"	"	$34^1/_2$	"	12	"	"	"	"	26	"
29.8	"	"	"	"	5 hours		13	"	"	"	"	29	"
Cloudiness noted in lime water in $24^1/_2$ minutes							14	"	"	"	"	32	"
							15	"	"	"	"	$35^1/_2$	"
							Cloudiness noted in lime water in 23 minutes						

As was indicated in a previous experiment, the CO_2 evidently passes through the pinene layer into the underlying medium. Therefore, in order to ascertain the absorption power of pinene itself the following experiment was performed:

Five ccm. of pinene were placed in a dry tube and forced up by means of mercury. Fifty ccm. of CO_2 were then forced in with the following results.

1.4	ccm.	CO_2	absorbed	in	5	minutes
3.7	"	"	"	"	20	"
4.5	"	"	"	"	30	"

The absorption is very slow and small in amount indicating that the pinene itself possesses but little absorptive power in reference to CO_2.

SULPHUR DIOXIDE.

A series of experiments were also performed to determine the absorption of SO_2 in pinene.

Thirty-five ccm. of pinene were placed in the lower part of a Lunge nitrometer and forced up by means of water. Thirty-five ccm. of SO_2 were then forced in with results which show remarkable absorptive capacity on the part of pinene for SO_2. In $2^1/_2$ minutes all but 0.6 ccm. of the gas had been absorbed. The reaction

proceeded at such a rapid rate that it was impossible to determine the absorption rate of any intermediate volumes. The absorption became fairly constant when a volume of approximately 0.5 ccm. of gas remained.

Thirty-five ccm. of SO_2 were forced in a second time with the result that in $2^1/_2$ minutes all the SO_2 but 2.6 ccm. had been absorbed, the volume of unabsorbed gas remaining fairly constant at 1.4 ccm.

Thirty-five ccm. of SO_2 were forced in a third time. In $2^1/_2$ minutes all but 7.4 ccm. of gas had been absorbed, the volume of unabsorbed gas remaining fairly constant at 2.6 ccm. in 4 minutes.

Thirty-five ccm. of SO_2 were forced in a fourth time. All the 12 ccm. of SO_2 was absorbed in $2^1/_2$ minutes, the volume of unabsorbed gas remaining fairly constant at 3.4 ccm. in $5^1/_2$ minutes.

For the fifth time 35 ccm. of SO_2 were forced in, leaving but 15.2 ccm. unabsorbed in $2^1/_2$ minutes. The volume of unabsorbed gas became fairly constant at 4.9 ccm. in $6^1/_2$ minutes.

In order to determine the solubility of the SO_2 in water under like conditions, 50 ccm. of SO_2 were forced into a Lunge nitrometer filled with water. In $2^1/_2$ minutes 14.5 ccm. of SO_2 were absorbed, in 5 minutes 26.8 ccm and in 10 minutes all the gas was absorbed.

The same experiment was performed using 35 ccm. of SO_2 in place of 50 ccm. In $2^1/_2$ minutes 12.4 ccm. of SO_2 were absorbed and in 5 minutes 24.9 ccm. All the gas was absorbed in $7^1/_2$ minutes.

As the solubility of SO_2 in water is great, experiments were performed to demonstrate the solubility of SO_2 in pinene itself. In these experiments the pinene was placed in a dry, clean nitrometer and forced to the upper portion of tube by means of mercury. Five ccm. of pinene were used with 50 ccm. of SO_2. Results are as follows:

	Ccm. SO_2 absorbed.		
Time in minutes.	I.	II.	IIA.
1	15.6	15.0	2.8
2	25.8	25.6	5.2
3	33.4	34.0	7.6
4	38.0	39.0	9.3
5	41.6	42.3	10.5
6	44.0	44.6	11.7
7	45.5	45.9	12.5
8	46.5	46.7	13.0
9	46.9	47.1	13.5
10	47.1	47.4	14.0
20	..	..	16.0
45	..	..	17.6
60	..	..	18.3

Column IIA records results attained by passing 50 ccm. of SO_2 a second time into II.

The mercury supporting the pinene showed no evidence of any action of SO_2 upon it.

The pinene layer of these experiments became cloudy at the beginning of the experiment and finally became clear with a yellow color.

Part of the pinene layer was shaken vigorously with an aqueous fuchsin solution with the result that a purple precipitate was formed.

Upon boiling the pinene before adding the fuchsin solution no change was noted.

In order to establish the true relationship between pinene and SO_2 further experimental evidence must be submitted.

AMMONIA.

A series of experiments were carried out using ammonia gas.

In the first experiment 30 ccm. of NH_3 and 30 ccm. of pinene supported by water were used. The absorption was very slow, 3 ccm. of the gas being absorbed in 1 hour. The pinene layer became very cloudy at the upper portion. The water layer did not react ammoniacal with cochineal solution as indicator.

The experiment was repeated using water colored with cochineal solution. No change was noticed until a drop of water, which had adhered to the side of the tube, fell down into the water layer. A purple color was at once imparted to the cochineal water solution.

A third experiment was performed using the same volumes of pinene and ammonia gas, the pinene being supported by water (neutral in reaction) colored with cochineal solution. Extreme care was observed in preventing the water layer from coming in contact with the upper portion of the tube.

At the beginning of the experiment a cloudiness appeared at the surface of the pinene. This cloud gradually became denser and slowly settled, reaching the bottom of the pinene layer in $6^1/_2$ minutes. No change of color was observed in the cochineal layer.

In 20 minutes approximately 1 ccm. of ammonia had been absorbed. At this time the meniscus between the pinene and aqueous layers was disturbed but no change in color took place. Observations made after 30 minutes showed an absorption of 2.2 ccm., after 1 hour 3.8 ccm., and after 24 hours 7 ccm. At the expiration of 24 hours no change of color was discernible in the cochineal solution.

A part of the pinene layer, when agitated with cochineal solution, gave a very slight change of color although another part, after first having been boiled, gave no change in color.

This evidence, then, together with the fact that in the experiment the ammonia had not penetrated into the aqueous cochineal layer, would appear to indicate that the pinene held gaseous ammonia in solution but only in very slight amounts, and that evidently the majority of the gas had entered into reaction with the pinene. However, this latter statement requires further experimental data for confirmation.

The absorption of ammonia by pinene over mercury was also demonstrated. Five ccm. of pinene and 50 ccm. of gas were used. The absorption was very slow, proceeding at the following rate:

0.4	ccm.	NH_3	absorbed	in	5	minutes
1.0	"	"	"	"	10	"
1.2	"	"	"	"	15	"
1.3	"	"	"	"	20	"
1.4	"	"	"	"	30	"

SUMMARY.

The results incorporated in this investigation warrant the statement that pinene possesses an absorptive capacity for certain gases, in some instances to a very high degree. Whatever fact of chemical significance may be attached to this phenomenon remains to be investigated.

This investigation is to be regarded as a preliminary one for it is the intention to pursue the investigation further, using such gases as HCN, H_2S, N_2, NH_2OH, C_2H_4, C_2H_2, CO, etc., in order to obtain true physical and chemical constants.

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DIETHYLPHTHALATE.*

BY J. A. HANDY AND L. F. HOYT.

I. SUMMARY OF AVAILABLE SCIENTIFIC DATA IN THE LITERATURE.

Of the three possible isomeric diethyl esters of phthalic acid, the one of the present commercial importance is the diethyl ester of ordinary or orthophthalic acid. This ester was first prepared by Laurent[1] in 1836, who was also the first chemist to prepare phthalic acid by the oxidation of naphthalene. Laurent states:

"When one boils a mixture of alcohol ('wine spirit'), hydrochloric acid and phthalic acid (called by him 'naphthalene acid') in a retort there is obtained at the end of the distillation an oily material which remains behind in the retort. This oily material is heavier than water and I believe it to be the ester of phthalic acid, without, however, having obtained a sufficient quantity to make further investigation of it."

There is no question that Laurent actually made the ester, as the procedure he used is a standard laboratory method for ester formation.

Von Graebe and Born[2] in 1867 state that the only existing data regarding this ester are those of Laurent. Von Graebe and Born prepared the ester by the same process as used by Laurent, and, after carefully purifying it, found it to be a colorless and odorless oil, boiling at 295° C. (cor.), and having the elementary composition of $C_6H_4(CO_2C_2H_5)_2$. It may be noted in passing that this b. p. of 295° C., as determined by these chemists over 50 years ago, checks exactly with that of the commercial product on the market to-day.

Michael[3] in 1879 accidently prepared diethylphthalate by the action of phosphorus trichloride on monoethylphthalate which he was studying at the time. (The monoethyl ester is described by Michael as an oil, moderately soluble in water and unstable towards heat, decomposing on distillation into ethyl alcohol and phthalic anhydride.) Michael gives no data on the constants of the diethyl ester.

Von Graebe and Born[4] in 1883 studied further the ethyl and methyl esters of phthalic acid. They prepared the diethyl ester by three methods: (*a*) Ethyl iodide and silver phthalate, (*b*) sodium alcoholate and phthalyl chloride, and (*c*) phthalic anhydride and ethyl alcohol saturated with HCl gas. The esters obtained by these three methods showed the same b. p. of 294° C. at 734 mm., with the thermometer entirely in the vapor, and the sp. gr. (values not stated) differed only in the fourth decimal.

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* Read before Scientific Section, A. Ph. A., Cleveland meeting, 1922.

Brühl[5] in 1894 gives the physical properties of the diethyl ester, which he obtained from Kahlbaum. After drying over calcium chloride, and submitting it to fractional distillation, he found the great bulk of it to distil over sharply at 172° C. under 12 mm. pressure. At 752.5 mm. the ester distilled at 289° C. He also determined its density and refractive index for monochromatic light of different wave lengths as follows:

Sp. gr. $\frac{4.3°}{4°}$ = 1.1232

Sp. gr. $\frac{20.5°}{4°}$ = 1.1175

Refractive index, n, at 14.3° C.

Li—1.49999
Hα—1.50070
Na—1.50490
Tl—1.50960
Hγ—1.52498

W. H. Perkin[6] in 1896 found diethylphthalate to have a boiling point of 298–299° C. cor., to 760 mm. He determined its relative density at several temperatures, as follows:

$\frac{4°}{4°}$ C.—1.1358
$\frac{10°}{10°}$ C.—1.1306
$\frac{15°}{15°}$ C.—1.1268
$\frac{20°}{20°}$ C.—1.1234
$\frac{25°}{25°}$ C.—1.1205
$\frac{30°}{30°}$ C.—1.1178

In this same article, it might be of interest to note W. H. Perkin's[6] description of the other two isomeric diethylphthalates as follows:

"Diethyl ester of isophthalic acid, obtained by boiling the acid, alcohol, and ten percent of H_2SO_4 for seven hours is an oily liquid, b. p. 302° C. at 760 mm., m. p. 11.5° C., sp. gr. $\frac{15°}{15°}$ C. = 1.1289."

"Diethyl ester of terephthalic acid, obtained by adding absolute ethyl alcohol, a little at a time, to phthalyl chloride made by the action of PCl_5 on terephthalic acid, has a m. p. 43.2° C. and b. p. 302° C. at 760 mm."

Bogojawlenski and Narbutt[7] in 1905 prepared diethylphthalate by a rather unusual procedure of esterification in which they employed anhydrous copper sulphate as the condensing agent and claimed to have obtained a 67 percent yield of the ester from phthalic anhydride and ethyl alcohol.

No experimental data regarding the pharmacodynamics of diethylphthalate were found other than the general statements given in U. S. Patents 969,636 and 1,017,669, and in recent articles on specially denatured alcohol formula 39B in perfumery trade journals, stating that esters of orthophthalic acid are non-irritating and non-poisonous.

About twelve years ago, a German concern under the name of Dralle began manufacturing perfumes with diethylphthalate as a vehicle, instead of alcohol. This line met with considerable success at the time, and resulted in much experimental work along the same line here in America.

Shortly after this, a perfumer by the name of Rieger of California put on the market a line of perfumes known as "Rieger's Flower Drops," in which he used diethylphthalate as a vehicle, instead of alcohol.

About this time, Larkin Co. started its experimental researches on the use of this ester in obtaining colorless, non-alcoholic perfumes. The samples made at that time, and which we still have, show no signs of deterioration as to color, odor, etc.; however, this method was found to be very expensive and not as satisfactory, both from the standpoint of production and quality of product, as perfumes made with alcohol as a vehicle.

Long before this ester came into known use in this country, it was being used secretly under different trade names in synthetic perfumery compounds as an

adjusting agent for strength. One of its early specific uses was as a solvent for musk, in place of benzyl benzoate.

II. PATENTS ON THE USE OF DIETHYLPHTHALATE.

The importance and possible uses of diethylphthalate appear to have been realized in Germany over a decade ago.

On June 15, 1909, Hesse took out German Patent 227,667,[9] covering the use of the alkyl and aryl esters of phthalic acid, or their mixture, as solvents for fatty acids and ethereal oils, perfumes, etc., but especially for rosin and varnish gums, it being claimed the use of 30 parts by weight of diethylphthalate would give a perfect solution with 100 parts of rosin.

On May 19, 1911, Hesse took out German Patent 251,237,[10] an addition to the preceding patent, and patented the use of the "phthalic acid esters" as solvents for obtaining the natural perfumes by extraction, maceration, or diffusion, obtaining thereby perfume products which do not contain objectionable constituents and which dissolve completely and directly in alcohol even when diluted.

On February 20, 1912, U. S. Patent 1,017,669[11] was granted Albert Hesse of Wilmersdorf, Germany, as a new composition of matter, a solution of an organic perfume containing a phthalic acid ethyl ester, alcohol, and water as solvents. You can read the original application on page 61 of the *American Perfumer* for 1912. Although he used dimethylphthalate, as well as the ethylphthalates, he brings out that the phthalates are excellent solvents and act as fixatives in the prevention of irregular evaporation of perfume materials. This patent is now owned by the Chemical Foundation.

On September 6, 1910, U. S. Patent 969,636[8] was granted Dr. Kleber, now of Fritzsche Bros., on the use of the esters of orthophthalic acid as improved perfume bases in the manufacture of perfumery. This specifically set forth that the neutral ethyl esters of orthophthalic acid, including the diethyl ester, are colorless, practically odorless, have a low freezing point, are not readily inflammable, do not irritate the skin, and are non-poisonous; that they are miscible with alcohol, ether, chloroform, and glycerine in all proportions; that they are excellent solvents of various essential oils, balsams, synthetic compounds such as artificial musk, coumarin, and other substances used in the manufacture of perfumery; that they possess the properties of blending the various odoriferous materials in a satisfactory manner, as well as acting more or less as fixatives; that they are stable and without chemical action on the substances dissolved. On account of their high boiling points (275–325° C.), they volatilize very slowly but finally completely without leaving any stain on fabrics. This patent is now owned by Fritzsche Bros. Inc., New York City.

The *American Perfumer* for January 1922 published signed statements by both the Chemical Foundation and Fritzsche Bros., in which they generously waive any infringement under their respective patents, for the use of diethylphthalate as a denaturant in specially denatured alcohol formula 39B.

German Patent No. 313,059[12] covers the use of the ester salts of phthalic acid as glycerine substitutes.

In 1917, German Patent 302,581[13] was taken out, covering the use of the neutral esters of phthalic acid as heat-transmitting media, it being specified that these esters were mobile liquids, stable, non-inflammable, with a high boiling point (280–290° C.) and a flash point above 160° C.

III. RECENT ARTICLES AND EDITORIALS ON USE OF DIETHYLPHTHALATE AS A DENATURANT.

Within the past year numerous editorials and general statements have appeared in the journals of the Perfumery and Essential Oil trade.

In the special May 12, 1921, edition of the *Perfumers' Journal and Essential Oil Recorder*,[14] diethylphthalate is discussed as a denaturant for alcohol that would meet with universal satisfaction.

An article in the June 1921 edition (Vol. 1, No. 10, pp. 32–33)[15] of the same journal warmly supports the use of diethylphthalate, and quotes Dr. I. V. Stanley Stanislaus and Mr. Fries of Fries and Fries Co., manufacturing chemists, Cincinnati, as endorsing a two to three per cent solution of diethylphthalate in alcohol as a substitute for pure alcohol in the manufacture of perfumes and toilet waters. Dr. Stanislaus further stated:

"If the Department should adopt this new denaturant, it could regulate so that all of the U. S. P. and all the N. F. fluidextracts, tinctures and spirits could be made with the alcohol, because their doses range between 5 and 60 drops (about a teaspoonful is the major dose of a majority of these), and 5 to 30 drops dose of these preparations largely diluted with sweetened water could be taken without any injury to the patient, and without much inconvenience, whereas larger doses, of, say, half a wine glass full, would make the drinker sick."

A large amount of research work was carried on under the auspices of the Alcohol and Research Committee of the Manufacturing Perfumers' Association in collaboration with the Industrial Alcohol and Chemical Division of the Internal Revenue Dept., which finally resulted in the issuance by the Treasury Department of Pro-Mimeograph, Coll. No. 2840, on September 23, 1921, authorizing the use of specially denatured alcohol formula 39B, to wit:

"To every 100 gallons of pure ethyl alcohol add $2^1/_2$ gallons of diethylphthalate, for use in the manufacture of perfumes, toilet waters, alcoholic barber supplies, and lotions." The specifications for the diethylphthalate to be used in this formula are as follows: "Diethylphthalate is colorless, practically without odor and is miscible with alcohol. Boiling point 290–297° C. The ester content should be not less than 99 percent determined by the usual saponification method."

The American Perfumer, October 1921, p. 328,[16] carries an editorial which includes a reprint of the authorization by prohibition enforcement authorities of the new 39B alcohol, and a statement from Dr. I. V. Stanley Stanislaus that "the new alcohol when used in perfumes will not irritate the most sensitive and delicate skin. Its non-irritating qualities have been amply demonstrated." Dr. Stanislaus further states that it is a fact that for years the floral oils of Europe have been standardized by the use of diethylphthalate (much as dyes are standardized by the manufacturer with salt or Glauber salt). In this connection it is of interest to note that in 1920 there appeared an anonymous article[17] printed in the *Deut. Parfümerie Ztg.* in which it is claimed that diethylphthalate is extensively used as an adulterant of essential oils and mentions particularly the adulterations of the essential oils of anise, bergamot, cassia, violet, lavender, mint, and cinnamon. It is possible that in these cases diethylphthalate, if not present in an excessive quantity, was used for purposes of standardization rather than adulteration.

In the *Perfumers' Journal and Essential Oil Recorder* for January 1922, there is an article by F. H. Lowenfels.[18] The author states that there is a general impression in the trade that 39B alcohol cannot be used in foaming hair tonics where it is believed the ester will saponify in the alkaline solution used. Lowenfels states that as a matter of fact the ester is remarkably stable and will not saponify in a solution of the degree of alkalinity employed in hair tonics. Lowenfels claims, however, that 39B alcohol reduces the foaming power because of the effect of diethylphthalate on the surface tension of alcohol. He neglected to state, however, whether it increased or decreased the surface tension of the alcohol or the tonic.

Geo. A. Witmer, in *Ungerer's Bulletin*,[19] states that specially denatured alcohol formula 39B is the only denaturing alcohol up to the present time (April 1922) which has met with anything like general approval. However, he questions whether diethylphthalate in $2^1/_2$ percent solution in alcohol is a suitable denaturant for all perfumes, especially those composed of delicate floral ingredients.

A. B. Lyons, in his excellent article[20] on the "Detection of Diethylphthalate in Whisky," describes both a qualitative and quantitative method for diethylphthalate. Lyons' qualitative method involves an extraction of the ester by means of petroleum ether and its subsequent conversion into fluorescein by a procedure practically identical with the method which we have used and which is subsequently described in our paper as the modified Mulliken Test for Fluorescein.

ANALYTICAL DATA SHOWING COMPARISON OF STANDARD DOMESTIC DIETHYLPHTHALATES WITH TWO SAMPLES OF FOREIGN MANUFACTURE.

	Manufacturer.	Sp. gr. 15.6° C.	Refractive index 20° C.	Opt. act. 20° C.	Free acidity as phthalic acid, %.	Saponification number. Mgm. KOH per Gm.	Corrected for free acidity.
1.	Van Dyk.....	1.1236	1.5008	(−)0°, 26.4′	0.105	503.35 99.66% ester	502.54 99.50% ester
2.	A. Chiris.....	1.1232	1.5013	(−)0°, 2.0′	0.048	502.98 99.58% ester	502.63 99.51% ester
3.	Fritzsche Bros..	1.1261	1.5018	(+)0°, 3.6′	0.103	503.58 99.70% ester	502.96 99.58% ester
4.	C. E. Ising.....	1.1229	1.5020	(+)0°, 4.1′	0.049	500.82 99.16% ester	500.49 99.09% ester
5.	U. S. Ind. Alcohol Co.....	1.1222	1.5008	(+)0°, 5.1′	0.025	504.16 99.82% ester	503.99 99.78% ester
6.	The Rossville Company....	1.1220	1.5008	(+)0°, 1.2′	0.017	503.92 99.77% ester	503.81 99.75% ester
	Foreign						
7.	Morana Inc. (German)....	1.1239	1.5019	(+)0°, 6.2′	0.105	502.54 99.50% ester	501.74 99.34% ester
8.	Muhlethaler Co. (Swiss).....	1.1218	1.5014	(−)0°, 5.2′	0.020	501.30 99.25% ester	501.10 99.21% ester

Since the authorization of specially denatured alcohol formula 39B by the U. S. Treasury Dept. in September 1921, the Alcohol Committee of the American Manufacturers of Toilet Articles has been accumulating practical information on the efficiency of this formula in the manufacture of high-grade perfumes and toilet waters. It having been demonstrated that high-grade perfumes and toilet waters contain sufficient denaturing agents in the form of essential oils and other non-potable perfume bodies to render the alcohol unfit for beverage purposes when there in proportions of two percent and over, and whereas the diethylphthalate because of its viscosity and fixative properties tended to flatten somewhat the more delicate floral odors, and when used on the skin in the strength of $2^1/_2$ percent solution tended to hold the alcohol and certain perfume materials on the skin long enough to cause slight burning and irritating effect, especially with those who might have a sensitive skin, it was deemed advisable to obtain a reduction in the

amount of diethylphthalate from $2^1/_2$ percent to 1 percent as authorized in specially denatured alcohol formula 39C under Pro-Mimeograph Coll. No. 2993, issued by the U. S. Treasury Department on August 2, 1922, to wit:

"To every 100 gallons of pure ethyl alcohol add 1 gallon of diethylphthalate, for use in the manufacture of high-grade perfumes and toilet waters containing not less than 2 percent by weight of essential oils or their equivalent in perfume materials. The diethylphthalate used in this formula shall be of the same quality as that specified for use in formula 39B, and shall be free from chlorine."

"The Department will only permit the use of this formula by manufacturers who are properly equipped by reason of experience and manufacturing facilities to effectively control their manufacturing operations in accordance with the limitations governing the use of this formula."

ANALYTICAL DATA SHOWING RANGE OF THE MORE IMPORTANT PHYSICAL AND CHEMICAL CONSTANTS FOR ALL THE DIFFERENT SAMPLES.

Specific gravity/15.6° C.	1.1218 to 1.1261
Refractive index/20° C.	1.5008 to 1.5020
Optical activity/20° C.	(−)0°, 26.4′ to (+)0°, 6.2′
Free acidity as phthalic acid	0.017 to 0.105%
Saponification number mgm. KOH per Gm.	500.82 to 504.16
	99.16 to 99.82% ester
Saponification number corrected for free acidity	500.49 to 503.99
	99.09 to 99.78% ester
Boiling point at 734 mm. pressure	295° C. average temp.
Boiling point at 30 mm. pressure	182° C. average temp.
Boiling point at 14 mm. pressure	163° C. average temp.
Surface tension (Sample 2), static, dynes per cm./25° C.	42.5
Flash point (Sample 2). (Cleveland Open Cup Tester, A. S. T. M. model)	153.3° C.

DETAILED DESCRIPTION OF TECHNIQUE EMPLOYED IN OBTAINING FOREGOING CONSTANTS.

Specific Gravity.—Determined at $\frac{15.6°}{15.6°}$ C. by means of calibrated pycnometer provided with thermometer.

Refractive Index.—Determined at 20° C. on Zeiss refractometer. Refractometer calibrated with distilled H_2O and cedar oil, and corrections applied to readings of the samples.

Optical Activity.—Reported as degrees and minutes of angular rotation of a 2 dcm. column of the substance at 20° C., using sodium flame as a source of illumination. Instrument used was a Schmidt and Haensch polariscope, calibrated by the Bureau of Standards and certified to have an error of +0.7′ at 0° rotation. The 200-mm. tube used was No. 252, certified by the Bureau of Standards to have a length of 200.02 mm. at 20° C. The reported values for optical activity are the means of eight closely agreeing observations. The instrument was so adjusted that its observed correction at 0° was zero. The Bureau of Standards correction of +0.7′ (inherent error of the instrument) was applied to the observed readings.

Free Acidity.—Determined by dissolving weighed samples of about 3 Gm. in hot neutral alcohol, and titrating to a faint, permanent pink with $N/10$ NaOH, using phenolphthalein as indicator. Acidity is reported as phthalic acid, of which 1 cc $N/10$ NaOH = 0.0083044 Gm., on the basis of the 1921 atomic weights.

Phthalic acid, $C_8H_6O_4$ = Molecular wt. of 166.088
(Dibasic acid, equivalent weight = 83.044)

Saponification Number.—Mgm. KOH required to saponify 1 Gm. of the ester.

Diethylphthalate = $C_{12}H_{14}O_4$.

Atomic weights for 1921. *Jour. Am. Chem. Soc.*, August 1921, p. 1752.

C = 12.005 H = 1.008 O = 16.00 K = 39.10

Molecular weight of diethylphthalate = 222.172

Molecular weight of 2KOH = 112.216

Saponification number of 100.00 per cent diethylphthalate = $\frac{112.216}{222.172} \times 1000 = 505.086$

Saponification number of 99 percent diethylphthalate would be 500.03

Saponification number of the ester was determined, in duplicate, by accurately weighing about 2 Gm. into a flask from an acetylization apparatus, adding 50 cc $N/2$ alcoholic KOH from a calibrated pipette, boiling under reflux for one hour, rinsing apparatus with hot, neutral alcohol, and titrating while hot with $N/1$ H_2SO_4, using phenolphthalein as indicator, until the pink color was barely discharged. Duplicate blanks were run in exactly the same manner.

The $N/2$ alcoholic KOH was prepared according to U. S. P. IX, page 567, using Cologne Spirit. The final reagent resulting was water-white, which enabled the very accurate determination of the end-point in titrations, because of absence of any interfering colors.

The $N/2$ KOH was standardized with Merck's C. P. Potassium Bitartrate, dried at 120° C. 2.3518 Gm. of $KHC_4H_4O_6$ should require 25 cc exactly $N/2$ KOH to neutralize. Duplicate standardizations required 23.45 and 23.46 cc, respectively. Normality of the $N/2$ alcoholic KOH is, therefore, 0.53295 or 1.0659 $N/2$.

The $N/1$ H_2SO_4 used for back titration was standardized against the $N/2$ alcoholic KOH and its normality in very closely agreeing duplicate standardizations was found to be 1.0437 N. This standardization was also further verified by titration against an aqueous $N/2$ KOH standardized against benzoic acid purified according to directions of the Bureau of Standards.

Calibrated burettes were used, and the proper corrections to observed readings were applied.

Owing to its very high numerical value, the accuracy with which the saponification number of diethylphthalate may be determined, even when extreme care is used at every step, may be placed at about $^1/_{10}$ of 1 percent (numerically about 0.50 on a value of 505). To obtain values which would check to within 0.25 in duplicate determinations, using the same weight of sample (about 2 Gm.) it is necessary that the titrations check to within 0.01 cc $N/1$ H_2SO_4, or about $^1/_3$ of a drop. Since this is the ultimate limit of accuracy in reading a burette, it will be clear that the degree of accuracy stated above, *i. e.*, 0.1 percent, is about what may be expected and attained by working with great care.

NOTE: It is believed that no appreciably greater accuracy would result if the back titrations were made with a weaker acid, *i. e.*, $N/2$ or even $N/4$, on account of the fact that the end-point is the disappearance of a faint pink in a milky white solution (due to the insolubility of potassium phthalate in alcohol). In such a solution, the end-point is not quite so sharp or sensitive as in a water-white solution. A fraction of a drop of $N/1$ acid would, it is believed, enable the operator to secure a sharper end-point than could be obtained from the very gradual transition at the end-point which would result from the addition of fractions of drops of $N/2$ or $N/4$ acid.

Example of saponification number determination: 50 cc $N/2$ alcoholic KOH from the same calibrated pipette used in every case.

Cc $N/1$ H_2SO_4 (1.0437 N) for back titration.....	Blank No. 1	25.31 cc	No. 2 25.29 cc	Average, 25.30 cc
Sample diethylphthalate.....	Detn. No. 1	6.37	No. 2 6.11	
Difference: Blank minus back titration.....	No. 1	18.93 cc.	No. 2 19.19 cc	
Weight of samples.....	No. 1	2.1950 Gm.	No. 2 2.2275 Gm.	

Saponification number = $\frac{\text{Mgm. KOH consumed}}{\text{Wt. of sample in grams}}$

Saponification Sample No. 1 $\frac{18.93 \times 1.0437 \times 56.108}{2.1950} = 505.03$

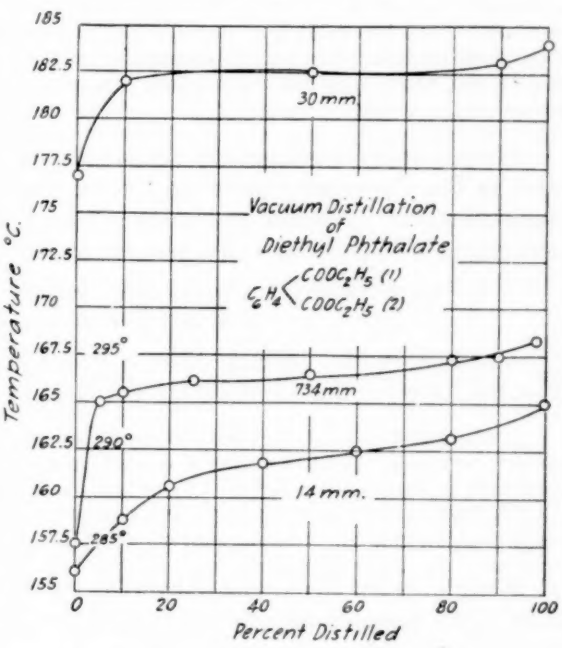
Saponification Sample No. 2 $\frac{19.19 \times 1.0437 \times 56.108}{2.2275} = 504.50$ Average, 504.760

$\frac{504.760}{505.086} \times 100 = 99.93$ percent diethyl ester

NOTE: A difference in titration of 0.01 cc $N/1$ H_2SO_4 changes the value of the saponification number by 0.25.

Boiling Point.—Distillation test: 250-cc quantities of standard commercial diethylphthalate were distilled from a 500-cc Claisen distilling flask provided with a Tycos precision grade No. 360,771 nitrogen-filled thermometer in the side tubulation, and connected with a Graham water condenser. The entire flask was heavily lagged with asbestos and heat was supplied by an electric flask heater equipped with rheostat. A Cenco Rotary Vacuum Pump was used for the vacuum distillations, together with a special graduated Fuch's Vacuo receiving flask.

Boiling Point.—Distillation (*a*) at 734 mm. pressure: The actual barometric reading on the day the distillation was made. Rate of distillation—approximately 5 cc per minute. The first drop came over at 285° C. After 98 percent had distilled over, the temperature was 295.8° C., which was taken as the end-point. The average distillation range for the various samples tested was about 3° C., with about 65 percent of the sample distilling between 294° and 295° C., under the conditions prevailing at the time of this test. All samples turned yellow in the distilling flask during the boiling. Although the distillate was practically water-white, it had a pronounced still odor. There was about two percent of dark residue left in the flask at the end-point. In commercial practice, diethylphthalate is always distilled under vacuum as there is always some slight decomposition on prolonged boiling of compounds of this nature at high temperature.



Distillation (*b*) at 30 mm. pressure: About half an hour was required after starting vacuum and heat before the first drop came over. When a uniform heat had been established, distillation proceeded at the rate of 4 cc per minute. At this pressure, the boiling point over the bulk of the range of distillation was quite constant. The first drop came over at 177° C. and the last portion at 184° C. The bulk of the distillate between ten and ninety percent distilled within the range of 182° to 183° C.

Distillation (*c*) at 14 mm. pressure: The same degree of heat was applied as in distillation (*b*). There was a continual slight rise in distillation temperature, the first drop coming over at 156° C. and the last portion of the distillate at 165° C., the rate of distillation being 7 cc per min-

ute. The bulk of the distillate between 15 percent and 85 percent distilled within the range of 160–163° C. The foregoing curves show the distillations more clearly.

Surface Tension.—The static surface tension of diethylphthalate was determined with a Du Nouy Tensimeter which was standardized against redistilled water. The following values were found:

		Static surface tension dynes per cm./25° C.
1.	Redistilled water	75.9 (note)
2.	Diethylphthalate (lab. sample)	42.5
3.	Cologne Spirit (lab. sample)	27.6
4.	39B alcohol made from (2) and (3)	27.9
5.	39B alcohol, commercial sample	27.9
6.	39C alcohol, made from (2) and (3)	27.7
7.	39C alcohol, commercial sample	27.7

NOTE: The value of 75.9 dynes per cm. for the surface tension of water at 25° C. (which was checked exactly on different days) is slightly lower than the value of 77 dynes per cm. at 25° C. reported by Du Nouy (*J. Gen. Physiology*, 1, 521, 1919). Dicks, in an unpublished thesis, working at M. I. T., found, however, the surface tension of conductivity water (specially purified distilled water) to be 79.5 dynes per cm. at 20° C. with the Du Nouy Tensimeter. This value is equivalent to 78.7 dynes per cm. at 25° C., or 1.7 dynes higher than the value found by DuNouy. These variations may be due in part, at least, to slight variations in the circumference of the 4-cm. platinum wire rings supplied with the different tensimeters. Harkins (*J. Am. Chem. Soc.*, 49, 499, 1919), using different methods, arrived at a value of 73 dynes per cm. for the static surface tension of distilled water.

Flash Point.—A commercial sample of diethylphthalate was tested for flash point in the Cleveland Open Cup Tester, latest American Society for Testing Materials model. When heated at the standard rate of 5° C. per minute, duplicate tests gave a flash point by this apparatus of 308° F. or 153.3° C.

1. DETECTION OF DIETHYLPHTHALATE BY THE MODIFIED MULLIKEN TEST FOR FLUORESCEIN.

Mulliken, in his "Identification of Pure Organic Compounds," Vol. 1, p. 84, gives the following directions for the detection of phthalic acid:

> "Mix 0.05 Gm. of the powdered acid with an equal quantity of resorcin. Place in a dry test-tube and moisten with one drop of concentrated sulphuric acid. Stand the test-tube in a liquid bath at a temperature of 160° C. and heat for three minutes. Cool, treat the fused mass with 2 cc dilute sodium hydroxide solution; pour into 500 cc of cold water. The water will show a very intense yellow-green fluorescence due to fluorescein."

When tried out on phthalic anhydride, the above test gives an intense yellowish green fluorescence, unobscured by the reddish brown color so prevalent from the official caustic soda fusion.

It was possible to modify the test as described by Mulliken to cover the detection of minute amounts of diethylphthalate, by "fixing" the phthalic acid from the ester with caustic as in the Linder test, and then adding an excess of 1.84 H_2SO_4, 0.05 Gm. resorcin, and heating three minutes at 160° C.

This procedure is very similar to that of Lyons, except that in our method no preliminary extraction of the sample with petroleum ether was considered necessary. Experiments in our laboratory have shown that extraction of 39-B alcohol with petroleum ether, according to Lyons' procedure, is practically quantitative, as

claimed by Lyons. In samples containing carbohydrate material, this preliminary extraction of the diethylphthalate would be advisable.

In testing liquid products like denatured alcohol, perfumes, and whisky, the extraction process is merely an extra, unnecessary step. In the case of perfumes, the petroleum ether has been found to extract a large proportion of the perfume oils. The same results, however, are obtained by testing a sample of perfume directly, as when a petroleum ether extract of the sample is used.

In cases where a large amount of aromatic bodies, resins, or other organic extractive matter is present, the following procedure can be used to advantage: Extract the sample with petroleum ether, evaporate the solvent, and saponify the ether extract with an excess of $N/2$ alcoholic KOH. If the diethylphalate is present, there will be formed white needle-like crystals of potassium phthalate which can be filtered off and treated with resorcin and sulphuric acid as described below.

Full directions for the test are as follows:

"To 10 cc of 39B alcohol or 5 drops diethylphthalate in a small casserole or evaporating dish, add 5 cc of 10 percent NaOH solution, and evaporate virtually to dryness on the steam-bath. Remove the dish from the bath, cool, and cautiously add 2 cc 1.84 H_2SO_4, a drop at a time, from a pipette, covering with a watch glass if necessary to avoid spattering. Pour the resulting solution at once into a dry test-tube containing 0.05 Gm. of resorcin, stand the test-tube in an oil-bath heated to 160° C. and maintain at that temperature for 3 minutes. Remove the test-tube from the bath, allow it to cool, and transfer a small portion of the contents to a large test-tube containing 50 cc H_2O made alkaline with 5 cc of 10 percent NaOH. The characteristic color of fluorescein develops at once, if the above quantities of 39B alcohol or the ester are used. A blank run in precisely the same manner should give a pale amber- or straw-colored solution free from fluorescence."

Caution: When the test is run on floral essences it frequently happens that a greenish blue or greenish red bloom appears when no diethylphthalate is present. Care should be observed not to confuse this bloom (or pseudo-fluorescence) with the intense yellowish green fluorescence of true fluorescein. It is well, in testing unknowns, to run a control test with a genuine sample of the ester, 39B alcohol, or phthalic anhydride, in order that one may have a sample of genuine fluorescein to compare with the colors given by unknowns.

When the test is being made to detect very small amounts of the ester, it is advisable to pour the entire melt into 500 cc of water containing 50 cc of 10 percent NaOH. Working with great care and using absolutely clean utensils it is possible to detect with certainty 0.1 mg. of diethylphthalate in alcohol when no interfering substances are present.

The modified Mulliken test was applied to small amounts of 39B alcohol. One cc of the 39B with 9 cc Cologne Spirit gives the test with nearly the same intensity as the 10 cc quantity of 39B; 0.1 cc of 39B alcohol with 9.9 cc Cologne Spirit gives a very distinct positive test; and even 0.01 cc of 39B yields recognizable fluorescence by this test.

2. DETECTION OF DIETHYLPHTHALATE IN PERFUMES AND TOILET WATERS.

The modified Mulliken test was applied to several different standard types of odors, including Violet, Rose, Lilac, and Essfloral (Bouquet) Perfumes and Toilet Waters on samples with and without the diethylphthalate denaturant. In each case the test was either negative or positive, depending upon whether the diethyl-

phthalate was absent or present. The Violet and Rose products, however, contain substances which give rise to a reddish green fluorescence resembling the bloom of a mineral oil. This bloom is entirely different from, and of much less intensity than, the yellowish green fluorescence produced by these products when the diethylphthalate was present.

3. CONTRACTION OF ETHYL ALCOHOL AND DIETHYLPHTHALATE MIXTURES.

Solutions were made up by adding 1 percent and $2^1/_2$ percent by volume of diethylphthalate to 250 cc of Cologne Spirit in a 250-cc volumetric flask provided with stem graduations of $^1/_{10}$ cc from 250 cc to 280 cc. The flasks, alcohol, and ester were all at the same temperatures of 25° C., and the diethylphthalate was added by means of a calibrated graduated pipette. The following table shows the total contraction in volume:

Vol. of Cologne Spirit, cc.	Cc diethylphthalate.	Vol. of mixture, cc.	Contraction. Cc.	Contraction. Percent of total vol.
250	2.50	252.4	0.1	0.04%
250	6.25	256.0	0.25	0.10%

4. COMPARATIVE EFFECT OF COLOGNE SPIRIT AND 39B ALCOHOL ON THE FOAMING OR LATHERING POWER OF SOAP AND SAPONIN.

This was determined by means of a special graduated cylinder used in determining the comparative lathering power of soaps. The results tabulated in the following table show that while Cologne Spirit in low concentration causes an increase in lather, 39B alcohol has a marked inhibitory effect on the lathering or foaming power of soap and saponin solutions. This observation coincides with Lowenfels'[18] statement regarding the effects of 39B on foaming hair tonics.

(A) Soap. 1 cc of 20 percent liquid soap used in each test.
Total volume of liquid—100 cc used in each test.

Dist. H_2O, cc.	Cologne Spt., cc.	39B, cc.	Vol. lather, cc.	Percent change.
99	0	0	405	....
89	10	0	455	12 percent increase
89	0	10	120	70 percent decrease
74	25	0	190	53 percent decrease
74	0	25	0	100 percent decrease

(B) Saponin. Ten cc of a solution of 0.2 Gm. saponin (Merck's purified) in 100 cc dist. H_2O used in each test.

90	0	0	170	....
80	10	0	230	35 percent increase
80	0	10	0	100 percent decrease

SUMMARY.

Of all the esters of phthalic acid, the diethyl has proven to be the most satisfactory, so far, for use as a denaturant for perfumes and toilet preparations for the following reasons:

1. Because of its stability and freedom from color and odor. (The ethyl and methyl phthalates are readily decomposed upon heating.) It acts as a fixative, giving more uniform evaporation and lasting quality to odors.

2. Its ready miscibility and sufficient volatility, as well as high boiling point,

enable it to serve as both a volatile and non-volatile key in establishing the identity of specially denatured alcohol 39B and 39C.

3. It possesses a bitter, acrid, and numbing taste which renders the spirit unfit for beverage purposes in one percent solution.

4. It leaves no sediment and is a natural constituent of many perfumes because of its presence as a solvent and adjusting agent in many of the synthetic perfume materials.

5. It is not poisonous or toxic when applied to the skin. It possesses the slight antiseptic quality of the phthalic group and takes off the drying and slightly caustic action which pure alcohol leaves on the skin.

6. Its chemical test of identity is positive and easily carried out.

7. Diethylphthalate of exceptionally high purity and standard quality is being produced commercially in this country by several reputable manufacturers, at a reasonable price.

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THE STATUS OF DRUG-PLANT GROWING IN THE UNITED STATES IN 1921.

BY W. W. STOCKBERGER.

In 1921 the commercial cultivation of drug plants occupied a much less favorable position than that reported for 1918. Following the renewal of imported supplies this industry promptly reacted to the general principle that the production of any article declines as the price drops. The medicinals which were successfully grown during the World War were still produced in 1921 but in relatively unimportant quantities.

The drug gardens maintained by schools of pharmacy in various parts of this country which number 25 have continued to be centers of much popular interest, and, aside from their primary educational function, have rendered a distinct public service through the dissemination of practical information on drug-plant culture gained through experience.

A CONCENTRATED DAKIN'S SOLUTION.

BY ADRIAN THOMAS.*

During the war it was proven that Dakin's solution was a very valuable preparation for the treatment of certain surgical cases such as gunshot wounds. It was also pointed out that it could be very useful in the treatment of many other surgical cases which were not free from infection. The great difficulty with Dakin's solution is that it has been found difficult to prepare and that it must be prepared immediately before use because of its rapid decomposition.

Dakin's solution[1] as originally prepared is a solution containing from 0.4% to 0.5% sodium hypochlorite. It also contains sodium carbonate, and sodium borate or sodium bicarbonate. The alkalinity of Dakin's solution must be between certain limits and the alkalinity specified is that which will give no color with powdered phenolphthalein. However, it should give a momentary red flash when a drop of an alcoholic phenolphthalein is added. The presence of the sodium carbonate and bicarbonate has a buffer effect and keeps the alkalinity correct.

Several preparations all of about the same quality have appeared from which it has been claimed a correct Dakin's solution could be prepared by adding water to make the proper dilution. At least one claims to possess a different quality as well as a lower alkalinity than Dakin's solution and therefore to be less irritating. However, all of the preparations examined have shown a distinct alkalinity with solid phenolphthalein. The different quality of alkalinity referred to is presumably the alkalinity caused by calcium hydroxide. They have sodium salt present and consequently it may be expected to find some sodium hydroxide. True Dakin's solution contains no calcium and a definite limit is placed upon the alkalinity which is due to carbonates. If a sodium bicarbonate solution is added to these preparations the hydroxides are converted into carbonates and the excess of bicarbonate, acting along with the carbonates as a buffer, will tend to maintain the correct alkalinity, but at the same time it causes the calcium to precipitate. The presence of calcium does not appear to have any practical value, it merely gives opportunity for the claim that the alkalinity is of a different nature, but it does possess the disadvantage of causing a precipitate if sodium bicarbonate is added to correct the alkalinity.

The ideal preparation would be a concentrated solution of sodium hypochlorite in such form that by the mere addition of water a solution meeting all the requirements of Dakin's solution would be produced, but this is not possible because of the unstability of sodium hypochlorite.

To keep for any length of time sodium hypochlorite solution must be rendered considerably alkaline with either sodium hydroxide, sodium carbonate or other strongly alkaline substances. Also, the concentration of the hypochlorite must not be too great. Concentrated solutions of sodium hypochlorite decompose more rapidly than more dilute solutions and this decomposition increases with the concentration as a geometric function and not algebraically.

In August 1919, some experiments were begun to determine under what conditions a concentrated Dakin's solution would be most stable. In all, nineteen

* Section on Practical Pharmacy and Dispensing, A. Ph. A., Cleveland meeting, 1922.

[1] "Handbook of Antiseptics," by Dakin & Dunham, The Macmillan Co., New York, 1918.

solutions were made as stock solutions. Numerous dilutions of these stock solutions were made to determine the stability of the diluted solutions, their alkalinity, etc.

The most simple method of preparing a solution was found to be that of passing chlorine gas into a *cold* solution of sodium hydroxide until practically no color was imparted to a sample by adding powdered phenolphthalein and then adding sodium hydroxide solution to give the desired degree of alkalinity. Care must be taken to prevent addition of an excess of chlorine.

The large majority of these solutions were found to deteriorate very rapidly because of their high concentration, while a few showed a very slow deterioration, these being more dilute. It is impossible to prepare a hypochlorite solution which will not deteriorate to a certain extent, that is, with our present knowledge of the substance. We can only hope to find the conditions under which the decomposition is slow enough to permit us to keep the product a reasonable length of time.

Preparations may be made that will keep two or three years and be usable at the end of that period.

In the following table the results obtained with some of the solutions prepared are given. The concentration in percentage of sodium hypochlorite when freshly prepared, the concentration after standing twenty-seven months, the percentage loss per month and the alkalinity are given—the alkalinity being the number of cubic centimeters of tenth-normal hydrochloric acid required to discharge the color produced in ten cubic centimeters of the solution by powdered phenolphthalein.

Laboratory no. of prep.		Initial conc.	Concentration after standing 27 months.	Percentage loss per month.	Alkalinity cc $N/10$ HCl to discharge color produced with powd. phenolphthalein in 10 cc.
NaOH + Cl_2	10	4.82	2.75	1.59	5.4
NaOH + Cl_2	11	2.94	2.24	0.88	3.9
NaOH + Cl_2	12	2.51	2.04	0.69	3.4
NaOH + Cl_2	13	2.04	1.76	0.51	3.5
NaOH + Cl_2	14	1.51	1.40	0.27	3.2
NaOH + Cl_2	15	4.61	2.72	1.52	9.9
NaOH + Cl_2	16	2.79	2.12	0.89	6.3
NaOH + Cl_2	17	2.33	1.89	0.69	5.9
NaOH + Cl_2	18	1.87	1.59	0.55	5.1
NaOH + Cl_2	19	1.39	1.27	0.32	4.0

The most suitable concentration of hypochlorite was found to be about 1.5%. This concentration requires two volumes of diluent for each volume of concentrated solution to give the proper concentration for clinical use. It is about the same concentration as the "Stock solution" usually obtained by the Dakin method, yet it is sufficiently dilute to prevent too rapid decomposition. The proper alkalinity appears to be between 3 and 3.5. This is sufficient to preserve the solution, yet when diluted with two parts of a 1% solution of sodium bicarbonate the specified alkalinity of Dakin's solution is obtained.

Dakin's solution has the advantage over some of the other chlorine disinfectants in that it will dissolve pus and necrosed tissue. Unlike some preparations of a similar type this Dakin's solution is not intended for use as a general disinfectant, but is intended for surgical use. By diluting with sodium bicarbonate a

product is obtained which does not give a precipitate that must be removed, and which meets the requirements of a true Dakin's solution.

This preparation when diluted with sodium bicarbonate is not a substitute for Dakin's solution nor is it superior to Dakin's solution, but it *is* a Dakin's solution in that it contains the same materials as the original Dakin's solution though the method of preparation is different. The inert salts will not be found in this preparation in exactly the same quantity as in the original Dakin's solution, but in the latter it will be noted that the proportion of inert salts is not always constant.

The advantage of this preparation over Dakin's solution prepared by the usual methods whenever it is needed, is that no titration or testing is required to produce a Dakin's solution for clinical use, after the concentrated solution has been prepared. It is only necessary to dilute the concentrated solution with a one per-cent solution of sodium bicarbonate and it is ready for use. The advantage of this preparation over similar preparations is that no precipitate is caused when the alkalinity is adjusted by the addition of sodium bicarbonate.

Formula and directions for making Dakin's solution as described above are as follows:

CONCENTRATED DAKIN'S SOLUTION.

Decanormal sodium hydroxide	50 cc
Chlorine gas	q. s.
Water q. s. to make about	1000 cc

Fifty cc of cold decanormal sodium hydroxide are diluted to 320 cc. Into 300 cc of this solution pass just sufficient chlorine gas so that a sample will give no color upon the addition of powdered phenolphthalein. An excess of chlorine must be carefully avoided. Add q. s. of the remaining 20 cc to produce a distinct red color when solid phenolphthalein is added to a sample; 10 cc of the solution should require not over 5.0 cc tenth-normal hydrochloric acid to neutralize, using solid phenolphthalein as an indicator. Determine hypochlorite content by method given in U. S. P. for assay of the chlorinated lime, using 5.0 cc of the solution. The number of cubic centimeters of tenth-normal sodium thiosulphate used multiplied by 0.0744 gives the percentage of hypochlorite. Dilute with q. s. water to reduce the hypochlorite content to 1.5% plus or minus 0.05%. Adjust alkalinity so that ten cubic centimeters of this concentrated Dakin's solution will require not less than 3.0 cc nor more than 3.50 cc of tenth-normal hydrochloric acid to discharge the color produced by solid phenolphthalein. (Titrations for alkalinity must be made rapidly as the hypochlorite will bleach the indicator in the course of time.) This stock solution should keep at least a year without appreciable loss of strength.

DAKIN'S SOLUTION FOR SURGICAL USE.

Conc. Dakin's solution	334 cc
1% Solution of sodium bicarbonate q. s. to make	1000 cc

This solution must give no color with solid phenolphthalein and but a momentary pink flash when a drop of alcoholic phenolphthalein solution is added to a sample.

PAPER NO. 8,
CHEMICAL RESEARCH DEPARTMENT,
PARKE, DAVIS & COMPANY.

THE SECTIONS OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

ABSTRACT OF MINUTES OF THE SESSIONS HELD IN CLEVELAND, AUGUST 14–19, 1922.

SCIENTIFIC SECTION.

The first session of the Scientific Section, A. Ph. A., was convened August 15, by Chairman Heber W. Youngken. Vice-Chairman J. P. Snyder presided during the reading of the

CHAIRMAN'S ADDRESS.

This year we celebrate our eleventh anniversary as a distinct scientific unit within the American Pharmaceutical Association. From a comparatively small group of scientists at its inception, I have watched its growth until to-day its membership includes many teachers of pharmacy and its allied sciences in pharmaceutical institutions of this country, quite a number of scientific workers in government bureaus as well as manufacturing pharmaceutical and chemical houses, but, I regret to state, relatively few practicing retail pharmacists.

Among the objects for which the American Pharmaceutical Association was founded, as indicated in Article 1, Section 3, of its constitution, were improving the science and art of pharmacy by diffusing scientific knowledge among apothecaries and druggists, fostering pharmaceutical literature, developing talent and stimulating discovery and invention. In Article 1, Chapter 8, of the by-laws pertaining to membership in the parent body, we note mention first made of the eligibility of every pharmacist and druggist of good moral and professional standing. If we glance at Section 2 of the by-laws, dealing with membership in the Scientific Section, we note that all members of the American Pharmaceutical Association in good standing are eligible for membership. By far the major number of members in the parent body are practicing pharmacists. Why more of this larger group have not affiliated themselves with the Scientific Section and taken an active part in its proceedings is beyond my comprehension.

It is very evident that if pharmacy in this country is to attain a standing professionally on the par with law, medicine, pedagogy and engineering, more of its members who practice the science and art as retail pharmacists must participate in the scientific investigations of pharmaceutical problems and allign themselves with professional work.

While we have shown considerable growth as a section during these eleven years of our existence, there is still much to be desired. As our present membership falls short of three hundred, I would be derelict in my duty were I not to point out the wonderful opportunity now before us of individually soliciting new members for our Section from the retail and hospital pharmacist groups of the parent body. It is argued that most of these are unprepared for undertaking scientific research. While this may be true at the present, still I am enough of an optimist to believe that a goodly number are to be found with that latent talent outside of our fold, who, if given the proper encouragement, could be secured as active members. Once they are brought into our sessions, I think many could be induced to contribute to the progress of our work. Moreover, it must be borne in mind that with the increase in educational requirements and greater facilities for advanced work in pharmacy in many of our pharmaceutical institutions, we can expect a proportionate increase in the number of pharmacists qualified to attempt research.

The reaction of the great World War made its effects felt in the number of original investigations turned out by our members during the past several years. Judging from the long program of papers booked for this year's sessions of our Section, I feel that we have entered a renaissance in scientific research. I take this opportunity of thanking the numerous contributors to our program, many of the papers of which bear the stamp of painstaking effort.

If one takes the time to look over the contributions to our scientific sessions within recent years, one cannot help but be impressed with the increase in number of papers of biological and pharmacognostic significance. This can probably be explained in part by the increase in the number of teachers in these subjects in pharmaceutical institutions and also by the kindly spirit of helpfulness and encouragement that pervades our body.

Biology is becoming more and more recognized as a necessary branch in a well-rounded pharmaceutical curriculum. Biologists are more sought than ever before in helping to solve problems in connection with pharmaceutical and chemical research. We need more representa-

tives of this group of scientists in our Association and Section and could do much alike in increasing our membership and influence by providing a subdivision in our section for biology.

The keen interest shown year after year by the increasing number of pharmacognosists in our Section, as is constantly evidenced by the number of papers dealing with pharmacognosy that are being presented, merits a subdivision also of pharmacognosy.

I believe that it would be desirable to so amend the by-laws as to permit of the appointment, by the chairman of this Section, of sub-chairmen for the various divisions of scientific endeavor represented. We could thus create a stronger unit of the Scientific Section and more certainly assure a program adequately covering the entire field of pharmaceutical research.

The regular annual appropriation of $25.00 made by the parent body to this Section has during recent years been found insufficient for the carrying out of the work incumbent upon its officers. It would therefore be desirable to recommend that Article 1, Section 8, be amended to read, "The expenses of printing, mimeographing, postage and stationery shall be paid from the Association treasury, but in no case to exceed $50.00 for one year."

I believe our Section should from time to time propose honorary members who have distinguished themselves in pharmaceutical research. In this connection, I am thinking this year of the splendid work of Dr. L. van Itallie, chairman of the Pharmacopoeia Revision Committee of the Netherlands, and of Dr. Hermann Thoms, Director of the Pharmaceutical Institute in Berlin and member of the German Pharmacopoeia Revision Committee.

In conclusion, I desire to thank my associates for the wonderful coöperation they have given me in the past year's work. May the work of this Section shine as a star of the convention and may each of us carry away much of the usefulness and abundant enthusiasm for the duties of the coming year.

(Signed) HEBER W. YOUNGKEN.

A motion to refer the address to a committee of three was carried, and Vice-Chairman J. P. Snyder appointed Paul S. Pittenger, Anton Hogstad and E. E. Stanford. (The report of the Committee was made at a later session but for convenient reference is printed here.)

REPORT OF THE COMMITTEE ON CHAIRMAN'S ADDRESS.

Your committee has performed the duty assigned to it and begs to report as follows:

The Chairman's address contains four definite recommendations:

"*First Recommendation.*—Biology is becoming more and more recognized as a necessary branch in a well-rounded pharmaceutical curriculum. Biologists are more sought than ever before in helping to solve problems in connection with pharmaceutical and chemical research. We need more representatives of this group of scientists in our Association and Section and could do much alike in increasing our membership and influence by providing a subdivision in our Section for Biology.

"The keen interest shown year after year by the increasing number of pharmacognosists in our Section, as is constantly evidenced by the number of papers dealing with pharmacognosy that are being presented, merits a subdivision also of pharmacognosy."

The by-laws of the Association read as follows:

Article II.—To expedite and render more efficient the work of the Association, the following Sections are provided:

(1) Scientific Section, with four subdivisions: (*a*) Chemistry; (*b*) Botany and Pharmacognosy; (*c*) Biologic Assays; (*d*) Bacteriology.

Your committee approves of this recommendation and proposes that this Section ask that Article II, Sec. I of the by-laws of the Association be changed to read as follows:

I.—Scientific Section, with four subdivisions: (*a*) Chemistry; (*b*) Botany and Pharmacognosy; (*c*) Pharmacology and Biologic Assays; (*d*) Bacteriology and Biology.

"*Second Recommendation.*—I believe that it would be desirable to so amend the by-laws as to permit of the appointment, by the chairman of this section, of sub-chairmen for the various divisions of scientific endeavor represented. We could thus create a stronger unit of the Scientific Section and more certainly assure a program adequately covering the entire field of pharmaceutical research."

Your committee approves of this recommendation and proposes its adoption by changing the by-laws of the Scientific Section to read as follows:

SECTION III.—OFFICERS.

Article I.—The officers of the Section shall be a chairman, a first vice-chairman, a second vice-chairman, three sub-chairmen and a secretary selected from members of the Section.

SECTION IV.—ELECTION OF OFFICERS.

Article I.—The chairman of the Section shall at the first session appoint a committee of three who shall report to the Section at the same session two names for each office except the sub-chairmen.

SECTION V.—DUTIES OF OFFICERS—CHAIRMAN, VICE-CHAIRMEN AND SUB-CHAIRMEN.

Article I.—It shall be the duty of the chairman to represent the Section in the Council of the Association, to preside at all meetings of the Scientific Section as a whole and one of the sub-divisions, to appoint sub-chairmen for the remaining three sub-divisions, appoint all committees of the Section and fill any vacancies when occurring in these committees. He may present an annual address on any subject of interest to the Section that he may deem of sufficient importance.

No changes in *Articles II* to *IV*, inclusive.

Article V.—It shall be the duty of the sub-chairmen to assist the chairman to obtain members for the Section and papers for their sub-division, preside over the meetings of the sub-divisions, furnish to the secretary of the Section copies of all papers, discussions and minutes of the sub-division meetings.

"*Third Recommendation.*—The regular annual appropriation of $25.00 made by the parent body to this Section has during recent years been found insufficient for the carrying out of the work incumbent upon its officers. It would therefore be desirable to recommend that Section VIII, Article I, be amended to read, "The expenses of the printing, mimeographing, postage and stationery shall be paid from the Association treasury, but in no case to exceed $50.00 for one year."

Your committee approves this recommendation and proposes its adoption.

"*Fourth Recommendation.*—I believe our Section should from time to time propose honorary members who have distinguished themselves in pharmaceutical research. In this connection, I am thinking this year of the splendid work of Dr. L. van Itallie, Chairman of the Pharmacopoeia Revision of the Netherlands, and of Dr. Hermann Thoms, Director of the Pharmaceutical Institute in Berlin and member of the German Pharmacopoeia Revision Committee."

The Committee approves of this recommendation and would suggest that this Section propose the above names to the Council for election as Honorary Members of this Association.

Respectfully submitted,

(Signed) PAUL S. PITTENGER, *Chairman*,
E. E. STANFORD,
ANTON HOGSTAD.

The report of the Committee on President's Address was adopted. A recommendation was made that all purely research papers intended for the Scientific Section be presented in one group at one or more sessions arranged for by the officers of the Section, and that the authors be given every opportunity for full discussion of the papers. After considerable discussion the motion to adopt was tabled—the conclusion being that under the changes in the by-laws provision was made for the contemplated purpose of the recommendation.

Secretary Arno Viehoever reported on what had been done during the past year in obtaining a census of pharmaceutical research work, both as to published investigations and those under way in this country. He also called attention to other activities of the Section.

The report was received.

Chairman H. V. Arny reported on the Research Conference. The recommendations of the report were received and referred to the General Sessions (see Minutes of General Sessions).

A symposium on the U. S. Pharmacopoeia (now being revised) was part of this session's program. Chairman E. Fullerton Cook spoke of the progress of revision, the deletions and additions. He referred to the resumption of international pharmacopoeial work wherein there could be coöperation in the solution of many problems that come up in revising standards. Abstracts of organic chemical tests and some inorganic tests were distributed. The Chairman stated that other parts of the Pharmacopoeia were also well advanced toward completion.

As further publicity will be given to the subjects under discussion, publication is deferred and not included in these minutes.

The symposium was participated in by the officers of the Section, also by Messrs. Arny, Mansfield, Macht, Eldred, Caspari, Scoville, Diner, Kraemer, Nitardy, Schneider, Kebler, Pittenger, Fantus, Snow and others.

The National Formulary revision was presented by Chairman W. L. Scoville and is embodied in his report; however, in his remarks he spoke of the scope of the National Formulary and compared the work of its revision with that of the U. S. Pharmacopoeia.

The reading of papers followed. Discussions on the papers will accompany them when printed in the JOURNAL. Here, in the Minutes, only titles will be given; they follow:

"Color Standardization in the U. S. P.," by E. N. Gathercoal.

"Comparative Toxicity of a New Mercurial," by L. W. Rowe.

"Need of a Comparative Pharmacopoeia," by Otto Raubenheimer (abstract presented by Professor Cook).

"A Pharmacological Examination of Benzaldehyde and Some Benzyl Compounds Occurring in Nature," by David I. Macht.

"Relation between the Chemical Structure and Pharmacological Action of Atropine and Homatropine," by David I. Macht. (The two latter papers printed in this issue.)

"Tadpoles and Toxicity," by L. E. Sayre.

"Biological Standardization of Local Anaesthetics with Special Reference to Effects of Sterilization on Solutions of Cocaine and Procaine," by Paul S. Pittenger.

"The Effect of Large Doses of Cannabis Indica (Subjective Experiment)," by Albert Schneider.

"Proposed Pharmaco-Therapeutic Institutions and Obstacles," by F. E. Stewart.

"The Pharmacology of Pyrethri Flores," by W. H. Zeigler.

"Sodium Chloride," by H. L. Harris.

"Saccharin Feeding of Rats," by B. Fantus and L. Hektoen.

"New Aspects of the Toxicology of Arsenic," by E. W. Schwartze.

A motion was adopted that the Association take part in the Conference of Pharmaceutical Research, and that the required appropriation be made. It was referred to the House of Delegates and to the Council.

The following were appointed members of the Committee on Nominations: H. Engelhardt, *Chairman*, F. E. Stewart and W. L. Scoville.

The first session of the Scientific Section was then adjourned.

SECOND SESSION.

The second session of the Scientific Section was convened at 2:00 P.M., August 17, by Chairman Heber W. Youngken. The reading of the minutes of the first session was, on motion, dispensed with.

The Committee on President's Address reported. (It follows the Address, see Minutes of first session.)

Action on report of Committee on Nominations was deferred.

The first paper of this session was by Dr. H. H. Rusby on "Some Interesting Medicinal Plants of Bolivia." This is printed in the October number of the JOURNAL. Dr. Rusby was asked whether there was genuine coto bark on the market now. He stated that supplies could now be had. Dr. Arno Viehoever congratulated Dr. Rusby on his identification of the drug and determining sources of supply, and pointed out the importance of these discoveries to the manufacturers and laboratories.

Reading of papers was continued; titles of papers follow:

"The Histology of Vilca Bark," by Fanchon Hart (presented by Dr. Rusby). (This isssue.)

"Histology of Cocillana and Substitute Barks," by C. W. Ballard. (October JOURNAL.)

"Chemistry of Cocillana and Substitute Barks," by Harvey A. Seil (presented by Dr. Rusby). (Printed in this number of the JOURNAL.)

"A Garden of Herbs," by Caswell A. Mayo.

"The Drug Garden—Its Relation to the School of Pharmacy, State College and to Community," and "Nicandra Physalodes," by A. Hogstad, Jr.

"A Back Yard Pharmaceutical Garden," by E. E. Stanford.

"Analysis of One Hundred Present Day Alcoholic Beverages," by Henry Kraemer.

"On the Chemistry of the Seeds of Datura Stramonium" and "Constants of Cassia Leaf and Twig Oils," by Isao Nishimura and Edward Kremers.

"Balsam of White Fir," by I. Nishimura and Edward Kremers.

"Absorption of Gases by Pinene" and "Fractionation of Turpentine Oil," by W. F. Sudro and Edward Kremers. (Printed in this issue of the JOURNAL.)

"Hydroxylamine from Nitrosopinene," by J. A. Hall and Edward Kremers.

"New Guaiacol Derivatives," by Lina Winkelblech and R. E. Kremers.

"The Chemistry of Heptane and Its Solutions," by Edward Kremers.

"The Action of Light on Soluble Ferric Phosphate," by N. R. Mueller and Edward Kremers.

"Preliminary Note on Catnep Lactone," by O. H. Beath and Edward Kremers.

"A Microscopical Comparison of Some Official Herbs and Their Substitutes," by Fanchon Hart.

The second session of the Scientific Section was then adjourned.

THIRD SESSION.

The third session of the Scientific Section was convened by Chairman Heber W. Youngken, at 9 A.M., August 18.

The reading of Minutes was dispensed with.

Chairman Arno Viehoever of the Committee on Quality of Medicinal Products reported that the condition of imported drugs is, in general, much improved. He stated that a colleague of his, E. L. Schwarz, would present an interesting "Review of Crude Drug Imports for the Past Year at the Port of New York," and this would be published in the JOURNAL.

Reporter on the Progress of Pharmacy, H. V. Arny, presented his report. (See Minutes of the Council, October JOURNAL.)

The following papers were then read and discussed:

"Diethylphthalate," by J. A. Handy and L. F. Hoyt. (This issue of the JOURNAL.)

"Fluid Extract of Ergot," by J. P. Snyder.

"Pepsin—Method Used for Its Quantitative Estimation—Its Prominence and Effectiveness in Some of Its Preparations," by H. W. Vahlteich and E. J. Traut. (September JOURNAL.)

"Influence of Hydrochloric Acid in Cinchona Preparations" and "Hot Extraction," by W. L. Scoville.

"Work of the Pharmacognosy Laboratory, Bureau of Chemistry," by A. Viehoever.

"Studies of the Bark of Myrica Cerifera L.," by Heber W. Youngken.

"Phytochemical Notes," by C. L. Alsberg (presented by A. Viehoever).

"Kino, Gambir and Catechu," by E. N. Gathercoal and R. E. Terry.

"The Preparation of Acid-Fast Caramel," by Geo. D. Beal and Donald F. Bowee.

"Some Notes on Extract of Cascara and the Extraction of Cascara," by F. W. Nitardy.

"A Review of Contributions to the Literature of Pharmaceutical Botany and Pharmacognosy during 1921–1922 (August 1, 1921, to August 1, 1922)," by Heber W. Youngken.

"Electrometric Methods of Drug Assay," by W. J. McGill and P. E. Faulkner.

The following papers were read by title and referred to the Publication Committee:

"A Comparison of Cane and Beet Sugars" and "Concentrated Dakin's Solution," by A. Thomas.

"The Status of Drug Plant Growing in the United States," by W. W. Stockberger.

"The Occurrence and Forms of Calcium Oxalate in Official Crude Drugs," by Edgar T. Wherry and Geo. L. Keenan.

"Inorganic Constituents of Vegetable Drugs" and "Uniformity of Powdered Drugs," by E. L. Newcomb.

"Aloin" and "Estimation of Nitroglycerin," by H. Engelhardt.

"A Review of Crude Drug Imports for the Past Year at the Port of New York," by E. L. Schwarz.

"The Resorcin Test for Methyl Alcohol," by A. B. Lyons.

"Deterioration of Tincture of Digitalis," by C. C. Haskell, D. S. Daniel and G. S. Terry.

"Colloidal Chemistry and Its Application to Pharmacy," by C. B. Jordan.

"Use of Precipitated Copper for Sterilizing Purposes," by Gretchen Sprecher.

"Solution of Chlorinated Soda," by E. F. Kelly and John C. Krantz, Jr.

"Solubility of Chloroform in Simple Syrup and Other Syrups," "Stability of Elixir of Lactated Pepsin," "Suggestions for an Improved Formula for F. E. Glycyrrhiza," and "Petroleum Base for Ointment of Zinc Oxide U. S. P.," by F. J. Austin.

"The Identification of Some Local Anesthetics," by L. E. Warren.

"A Method for Assaying Ointment of Stramonium U. S. P.," by A. R. Bliss and M. F. Brown.

"An Assay for Elixir of Iron, Quinine and Strychnine, N. F.," by J. C. Krantz, Jr.

"Quantitative Determination of Sparteine in Tablets," by P. J. Jewel.

"A Review of Contributions to the Literature of Pharmaceutical Chemistry during 1921–1922," by W. O. Emery.

After receiving the report of the Committee on Nominations, the following were elected by ballot:

Chairman, Arno Viehoever, Washington, D. C.
Vice-Chairman, Paul S. Pittenger, Philadelphia, Pa.
Second Vice-Chairman, F. F. Berg, New York, N. Y.
Secretary, J. P. Snyder, Norwich, N. Y.

Retiring Chairman Heber W. Youngken thanked the members for the honor conferred and the support given him during his term of office.

Chairman Viehoever was glad to be associated with officers who had exhibited a growing interest in the Section. He was pleased with the success of the Section's work this year and hoped for a continuation and asked the support of the officers and members. He was followed by the other officers who expressed appreciation and gave assurances of continued efforts for the Section.

The Final Session of the Section was then adjourned.

SECTION ON EDUCATION AND LEGISLATION.

The first session of the Section on Education and Legislation was convened by Chairman W. H. Zeigler at 2 P.M., August 15. Secretary W. F. Gidley presided during the reading of the

CHAIRMAN'S ADDRESS.

I have little hope that I can add anything to what has already been embodied in the reports of past officers of this Section.

If we glance over the history of pharmacy that has to do with education and legislation, we may review, with satisfaction, the marked changes that have been made.

When I recall the educational conditions under which I commenced the study of pharmacy, twenty-five years ago, and the conditions that exist to-day, it would take many words to sum up the progress that has been made since then.

I shall not burden you with the repetition of a history that is well known to you, but shall confine myself to carrying out the provisions of Article 9 of the by-laws of the Association as it applies to the officers of this Section, *i. e.* "the compiling for reference enactments of the different states regulating the practice of pharmacy and the sale of medicines."

Several months ago, your chairman sent letters to the deans of all schools of the Conference, and the secretaries of all state boards of pharmacy, which read as follows:

> "As chairman of the Section on Education and Legislation of the American Pharmaceutical Association, I am sending a letter to the dean of each school in the Conference (secretary of each board of pharmacy in the United States) with the request that they kindly give me any information they may have relative to educational changes (legislation) affecting pharmacy in their state, which have been introduced in the past year.
>
> "I would also like to ask that you or any other member of the faculty (board) contribute a paper to our Section for the Cleveland meeting. Perhaps you have some suggestion that would be of interest to our Section.
>
> "Thanking you in anticipation of an early reply, I am, Yours very truly."

I have received thirteen answers from the deans of schools, and sixteen answers from the secretaries of boards.

A review of the answers of the secretaries of the boards does not reveal any marked changes

along legislative lines; this is due largely to the fact that there was no meeting of the Legislature in most of the states, during the past year.

Arkansas reports that beginning January 1, 1923, the law provides that each registrant of the boards shall pay in to the association $2 annually; it is their purpose to increase this to $5 per year, and also to introduce a bill at the next session of the Legislature convening January 1923, requiring all drug stores to secure a permit from the board of pharmacy before they may operate. This fund to be used for inspection purposes, and also in an effort to secure 100 percent membership in the American Pharmaceutical Association.

Colorado reports an unsuccessful attempt to pass legislation at the last session of the General Assembly.

New York reports that after January 1923 at least three years of high school or the equivalent will be required for admission to a registered school of pharmacy.

Massachusetts reports a bill passed by the present Legislature making the state law relative to the dispensing of liquor uniform with the federal and providing, additionally, a state license to be issued by the board upon recommendation of a local licensing board.

Wisconsin will introduce higher prerequisite requirements at the next session of the Legislature.

Virginia recently passed a modification Prohibition Law to the effect that no judge of the court may in the future issue a license to dispense whisky to any one other than a registered pharmacist. A prerequisite law requiring college graduation and four years of high school work became effective April 1. An unusual feature of the Virginia law is that drug store experience is not required in addition to graduation.

West Virginia reports a prerequisite law, effective January 1923.

Kansas reports that at the last meeting of the Legislature a bill was passed requiring graduation from a high school of candidates for examination as pharmacists.

Washington, D. C., reports a bill before Congress bearing on a matter of college attendance before candidates are eligible for examination.

The University of Minnesota College of Pharmacy reports that the abolition of the present three-year minimum course is under consideration, substituting for it a four-year course. It is interesting to note that the state pharmaceutical association addressed a request to the university to make the four-year course the minimum course.

I have pleasure in reporting that the school I am connected with, the School of Pharmacy of the Medical College of the state of South Carolina, increased its educational requirements for entrance to four years' high school, beginning with the session of 1922 and 1923.

A review of the reports from the schools of pharmacy of the state of New York shows that the College of Pharmacy of Columbia University is the only one of the schools that will require high school graduation for admission beginning with the session of 1923 and 1924, the other schools requiring three years.

A careful survey of the advances made along both educational and legislative lines shows, in my humble opinion, that we have a great deal to be thankful for.

Educationally, pharmacy has made even greater strides than its sister profession, medicine. There are many of us who can remember when, in some states, the course leading to the doctor's degree in medicine consisted of two years, of six or nine months each, without educational requirements for entrance.

The "Old-Time Pharmacist" of the *Druggists' Circular*, who said, "We are in an epoch of educational madness, and an over-production of men who believe in education to relieve them from work" has a queer conception of the value of education. If it is madness or folly to strive for the highest attainments in education, then, I say, let us be termed madmen. Education will make a street sweeper a better street sweeper; the boy with college and drug training is well balanced, and certainly better able to meet the contingencies of every-day life than one without such training.

There are several well-known conditions existing to-day in pharmacy, of which much has been said and written, that this Section should take cognizance of, *i. e.*, the alarming increase in the number of drug stores in the East and Middle West, and the number of applicants applying for registration in our schools of pharmacy.

That this condition does not exist in those states that had prohibition prior to the passage of the Eighteenth Amendment is thought by some to be an evidence in itself that a great many of

these so-called drug stores have been opened for the purpose of compounding prescriptions for alcoholics.

If this is true, this matter should be handled by this Section and the legitimate pharmacists, and the public should be informed of the fact that we object to this stigma being placed upon pharmacy.

To quote from the *American Druggist*, "It is a sad and lamentable fact that after years of effort at freeing the drug trade from so much of the evil attendant upon this business, it is getting back into the drug trade by leaps and bounds. It is imperative for various and manifold reasons that pharmacy should in some way, by hook or by crook, by fair means or by foul means, rid pharmacy of the liquor dispensing stigma. The argument to the effect that we retail druggists are obliged in some way to carry on this chore for the Government seems to me to be a mere fallacy, for I do not admit for one moment that the Government of the United States every intends any individual or body of individuals to participate in wholesale law violation."

This is no place to discuss whether the Volstead Act is a success or failure, what we do know is that it has been most unfortunate for professional pharmacy.

We are told by *The Northwestern Druggist* that more than a thousand drug stores have been opened in Chicago and in New York in the past two years.

The Minnesota Pharmaceutical Association has prepared a bill which provides for a licensing system for all drug stores.

If this bill should pass, the state board of pharmacy would have the power of granting permits for the opening of new drug stores—there must be a necessity or need of such a store. We await with interest the passage and the enforcement of this bill.

From the report made last year by Secretary Day, it seems that many of the schools in the Conference have had unusually large enrollments. It is my opinion that the pharmacy schools should actually set a limit on the size of their classes. We cannot effectually teach large classes.

It would be of interest to know if the teaching force has been augmented, providing that the class-room facilities are adequate.

To quote from the *American Druggist*, "One institution has a junior class that is by far the largest in the history of the school, more than we can conveniently accommodate." If the increase in attendance was confined solely to those schools requiring four years of high school work, I believe we could safely say that the unusual registration is due to the increase in entrance requirements. But an examination of the reports shows that the attendance has been equally great in those schools requiring only two or three years of high school work for entrance.

This situation should be closely watched and the committee on entrance of our institutions should do everything in their power to prevent undesirable students from enrolling.

There are two needs of vital interest to pharmacy that have been repeatedly discussed by this Section. I refer to higher prerequisite requirements, and higher educational standards for entrance to our schools of pharmacy. The committee on prerequisite legislation of the American Conference of Pharmaceutical Faculties has accomplished much along this line. To quote from a circular letter sent out this year by the chairman of this committee, "These prerequisite laws mark the progress of pharmacy. They enforce the better training of pharmacists. The passage of these laws is the one big progressive step of the decade."

The secretary of the N. A. B. P. also sent out a similar letter and a summary of arguments in favor of prerequisite legislation. This concerted action on the part of these two committees will undoubtedly produce results.

I am satisfied, after having served as chairman for the past year, that this Section is not serving its true purpose; for, while the statistics furnished by the chairman and the secretary yearly, as provided for by the by-laws, are of interest, a great deal more could be accomplished if the secretaryship was a permanent one and his duty, throughout the year, to keep in touch with the Committee on Prerequisite Legislation, and to watch carefully the federal and state laws affecting pharmacy—lending aid, financially and otherwise, to the enactment of legislation favorable to pharmacy; and also to defeat objectionable legislation.

Twenty-five dollars are appropriated annually to defray the expenses of this Section; this amount can be expended by the chairman or secretary alone in collecting the data for his report. If these two officers are to keep in touch during the year with legislative and educational enactments, the amount is certainly inadequate.

Two years ago I presented a paper before this body entitled "For the Good of the Public," the slogan for successful legislation. In this paper I stressed the point that in order to effectually present a bill in the interest of pharmacy, several factors are necessary; the most important being that the committee must be made up of men who are willing to leave their places of business, go to the capitol and stay there until they get what they want and, when they go before the committee on medical affairs of the Senate or House, they must do their best to convince the legislators that what they are asking for is for the good of the public, that the public must be protected, and it is not self-interest that prompts them to ask for their endorsement. After having served for several years on legislative committees, I am convinced that this is the keynote to successful legislation.

Let me remind you that at the New Orleans meeting a committee was appointed, known as the "Committee on Pharmaceutic Ethics," and that this committee is to report to this Section.

The present Code of Ethics of the American Pharmaceutical Association was adopted in 1852, and it is evident that it is in need of revision.

Quoting from an editorial by Clyde L. King—in May issue of *The Annals of the American Academy of Political and Social Science*—"Codes of ethics are important agencies for social control. The complexities and the specializations of modern industrial life leave many individuals unable to judge whether or not a member of any profession has performed his services with due regard to the interests of all, as well as with due regard to the interests of his client. In all but the crassest and most obvious defaults in service standards the work of the physician must be judged by physicians, and that of the lawyer by lawyers. And so with each of the professions. The higher the skill, the greater the need for organized group effort toward maintaining a fine sense of obligations, not primarily to others in the same profession, but chiefly to the general well-being of all."

If necessary an entire session of this Section will be given to a discussion of this important subject.

In conclusion permit me to gratefully acknowledge the honor conferred upon me as your chairman for the past year and at the same time to thank the officers and associates who have worked to make this meeting a success.

The address was referred to a committee consisting of Messrs. J. W. Sturmer, Willis Gregory and C. W. Ballard. They reported as follows:

Your committee commends heartily Chairman Zeigler's address, which, while it embodies no specific recommendations, does include an expression of his opinions on topics of vital interest to this Section. A spirit of optimism pervades his report on the progress pharmacy has made, and his thoughts on questions touched upon are well worth reading when the address appears in print. We would suggest in particular that the new officers of the Section consider them with the view to subsequent recommendations.

(Signed) J. W. Sturmer,
Willis Gregory,
C. W. Ballard.

REPORT OF THE SECRETARY.

The next order of business was the report of the secretary. This report was presented by Secretary W. F. Gidley. The tabulated statistical report is being prepared for publication, but will not be ready in time to be included in these Minutes and, therefore, will be printed in a later issue of the Journal, with the comments of the secretary. The following information is taken from the report: Total number of students in pharmacy schools last year, 5248; total number of high school graduates, 2608; total number of seniors in 4-year courses, 148; total students entering, 3073; high school graduates entering, 1067. Thirteen state boards of pharmacy will require high school graduation of candidates; 15 colleges of pharmacy will require high school graduation as an entrance prerequisite after January 1923. To a question by H. H. Rusby, Secretary Gidley replied that the figures were based on schools that reported; not all replied and only Conference schools were addressed.

Portions of Secretary Gidley's report follows:

Two years ago a large part of the work of the secretary of the Section on Education and Legislation was given direction by Prof. Edward Spease, who suggested the continued use of questionnaires by which information on both educational and legislative matters could be assembled, studied and progress noted.

This year your secretary has again used questionnaires and upon the replies from the same he has largely based his report.

The queries submitted encroached a few possible points upon the assumed work of certain standing committees of the American Conference of Pharmaceutical Faculties, and again overlapped in places the work presented in the H. C. Christensen chart. The latter overlapping, however, cannot be deprecated since the information presented is more recent by one year's time. But in large part the replies furnish material not supplied annually by any other agency.

The questionnaires were submitted to two groups, namely, the colleges and schools of pharmacy holding membership in the American Conference of Pharmaceutical Faculties, and the state boards of pharmacy through their secretaries.

The legislative work with which this Section is chiefly concerned, as we see it, is that which pertains directly or indirectly to the educational standards upon which pharmacy rests and with the coöperative work required to maintain or elevate those standards.

This Section is interested in *any* phase of *educational* work pertaining to pharmacy, be that teaching methods, examination questions, model methods of conducting examinations either by boards or faculty, higher standards, curricula, research, degrees, bulletins, pharmaceutical opportunities, publicity, rewards, scholarships, relation of the apprentice to his employer, etc., etc.

Coöperation was required to bring results from these questionnaires and that coöperation has not been found wanting. (Tabulated returns and questionnaires will be printed in a subsequent issue of the JOURNAL.)

The following are concluding statements of Secretary Gidley's report, and are immediately preceded by the omitted statistical matter:

In the light of my experience this year, I most heartily endorse Professor Spease's suggestion to have the president of the Association appoint a committee of one to control the distribution of papers among our Sections. Undoubtedly, papers are read in certain Sections which properly belong in quite a different Section. I also like the suggestion that the chairman of this Section outline a program for the year of all officers of the Section and that he assign topics on education and legislative matters to men capable of bringing in reports thereon to this Section. I believe also that the data collected by the secretaries of this Section should be brought together so as to present a composite record from year to year of the trend of education and educational-legislative matters of American pharmacy. Respectfully submitted,

W. F. GIDLEY, *Secretary.*

The report of the secretary was referred to the same committee to which was committed the address of the chairman. The report which was received follows:

Your committee recommends that the excellent report of the secretary be received by the Section on Education and Legislation, and that it be offered for publication in the JOURNAL of the Association. We believe that the statistics and conclusions embodied in the report are especially valuable in furthering the cause of pharmaceutical education.

We approve the suggestion that the president of the Association appoint a committee on the distribution of papers at the annual meeting in order that these papers will be presented before the proper section.

We approve the suggestion that the chairman of the Section on Education and Legislation outline the work of his associates and that he assign topics or request papers on given subjects from members who are capable and willing to assist in the activities of the Section.

(Signed) J. W. STURMER,
WILLIS GREGORY,
C. W. BALLARD, *Committee.*

Chairman Zeigler announced as the next order of business (special order) the report of the Committee on Pharmaceutical Ethics by Chairman Charles H. LaWall. (See JOURNAL A. PH. A., 10, 895 and 961, 1921.)

Chairman LaWall presented the report of the Committee; it follows:

REPORT OF COMMITTEE ON CODE OF PHARMACEUTICAL ETHICS.

Your committee, appointed at New Orleans to study the question of a suitable code of Pharmaceutical Ethics and bring in a report at this meeting, have given careful consideration to the subject and with the code proposed last year by the chairman of this committee as a basis

have consulted many members of the Association, both personally and by correspondence, and submit herewith a tentative code for discussion and possible adoption.

(Signed) LUCIUS L. WALTON,
R. A. LYMAN,
J. H. BEAL,
CHARLES H. LAWALL, *Chairman.*

The code was read paragraph by paragraph, and chapter by chapter, and discussed, a few changes and corrections were made and then by vote referred to the General Session, with a favorable recommendation for action and adoption. Messrs. J. H. Beal, Rusby, Gregory, Jordan, Finneran, W. C. Anderson, Meissner, Griffith, Stroup, Antonow, Frost, and others participated in the discussion. (Action of the General Session will be found in September JOURNAL, p. 717. The code of ethics is printed on pp. 728 and 729, of same issue.)

Nomination of officers followed.

The following papers were read and discussed:[1]

"Shall the Section on Education and Legislation Be Discontinued?" by William B. Day.

"The Relation of Education to Legislation," by L. E. Sayre.

"The Teaching of Qualitative Analysis in Colleges of Pharmacy," by C. B. Jordan.

"Full Time Officers of Instruction," by C. W. Ballard.

"Standardization of Education and Legislation," by B. Olive Cole.

"Why Not a Standard Label of Poisons?" by J. H. Beal.

A motion carried that this paper be referred to a Committee. (This Committee reported at a later session and action of the Association is reported on p. 718, September JOURNAL.)

"The Standardization of Schools of Pharmacy," by William B. Day.

The first session of the Section was then adjourned.

JOINT SESSION.

The Joint Session of the Section on Education and Legislation, American Conference of Pharmaceutical Faculties, and National Association of Boards of Pharmacy, was convened at 9:30 A.M., August 16, President L. L. Walton, of the N. A. B. P., presiding.

The first order of business was the reading of the report of the Fairchild Scholarship Committee by E. G. Eberle, Chairman. (See pp. 750–752, September JOUR. A. PH. A.) The report was discussed by Messrs. Sayre, Rudd, Lyman, Noll, Gregory, Sturmer, Bradley, Jordan, Snow, Diner, and others.

Chairman Theodore J. Bradley reported on the "Pharmaceutical Syllabus"—substance of the remarks is included in his report, printed in October JOURNAL, p. 817.

The following papers were read:

"Our Attitude toward Education," by Edward Spease.

"Progress in Pharmaceutical Education and Standards in the United States," by H. C. Washburn.

Then followed an open meeting:

C. M. Snow stated that an officer of the Department of Registration and Education of Illinois had tabulated the results of examinations of candidates for registration to practice medicine. These results he sent to the schools concerned so they might see wherein their graduates are deficient.

George Judisch asked whether a "College of Pharmacy" had been defined. Theodore J. Bradley replied that a definition is given in the application for membership in the American Conference of Pharmaceutical Faculties.

L. E. Sayre stated that responsive to a questionnaire—published and sent out to pharmacists of Kansas, which included the following questions: "Please state any grievances," "Discuss your grievances," "Please state what your opinion is as to the relation between medicine and pharmacy," etc.—he had received several replies and from these he would construct an editorial to be published in the JOURNAL OF THE A. PH. A. He believed that this editorial, based upon these communications, would be instructive and enlightening, and acceptable to the Association.

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[1] Discussions on papers will accompany these when printed in the JOURNAL, therefore omitted from these Minutes.

C. A. Dye stated that a definite program should be prepared for the Joint Session. Reference was made to the program of the Chicago meeting. No decided action was taken. The meeting was adjourned at 12:10 P.M.

SECOND SESSION.

The second session of the Section on Education and Legislation was convened by Chairman W. H. Zeigler at 2:15 P.M., August 18. Minutes of the preceding sessions were read and approved. A paper by W. F. Rudd, "The Virginia Experiment," was read and discussed. The paper and discussion will be published, but for reference it is stated that the experiment in legislation eliminates the practical experience requirement.

Secretary W. F. Gidley presented a paper by Otto Raubenheimer, in abstract, on "Standards of Articles Deleted from U. S. P. and N. F." The author suggests that such articles be still legally regarded as official—that a statement be placed in each book to that effect. Because of no standard such preparations differ in appearance, etc. After considerable discussion the paper was referred to the Committees on U. S. Pharmacopoeia and National Formulary.

A paper by C. B. Jordan, "Colloidal Chemistry and Its Application to Pharmacy," was read by title.

The following officers were elected for the ensuing year, and declared duly installed:

Chairman, W. F. Gidley, Lafayette, Ind.; *Secretary*, G. A. Bergy, Morgantown, W. Va.; *Associates:* H. L. Thompson, Salt Lake City, Utah; J. G. Beard, Chapel Hill, N. C.; H. L. Meredith, Hagerstown, Md.

The final meeting of the Section on Education and Legislation was then adjourned.

SECTION ON PRACTICAL PHARMACY AND DISPENSING.

The first session of the Section on Practical Pharmacy and Dispensing was convened by Chairman Ivor Griffith at 7:15 P.M., August 16. Secretary I. A. Becker presided during the reading of the

CHAIRMAN'S ADDRESS.

Fellow Members of the American Pharmaceutical Association:

You have done the unusual in selecting your humble servant as your chairman on two successive occasions, and I am pleased that the privilege is mine on this occasion at least to address you in person and not, by virtue of illness, by proxy.

The chairman of a Section runs contrary to our best traditions, who, overlooking what seems to be considered a bounden duty, fails to present the Section with what we are pleased to call an address. Fortunately the traditional standard governing the conduct of our several association affairs is not particularly definite in regard to the nature of the chairman's address—neither in point of quantity nor in point of quality, so that we are given somewhat of a free hand in its preparation.

And so, guarded by the conviction that there is no limit to the scope or length of this presentation, your chairman takes the shorter step and gives you ease of mind by prefacing his remarks with a kind reference to the brevity of his address.

Nor is the speaker cognizant of any particular change in his capacity to serve as a professional panacea purveyor since the mantle of chairmanship fell upon his shoulders. This apparent ability to give advice, and to remedy existing evils within and without the calling, seems to be a symptom of the disease called chairmania, which affects many persons entrusted with office. Your current chairman will endeavor, however, to subdue that pernicious symptom to the best of his ability for he conceives that the functions of a chairman are principally exercised in counting the yeas and nays, in blundering over parliamentary technic in arranging the program and in thankfully and delicately introducing his successors in office. To this platform he will religiously adhere.

However, so that we may not too drastically depart from the paths of our predecessors we beg to direct your attention to a few matters which are presently developing within our calling. He is indeed blind to the march of events who fails to see that the torch of the calling is not glowing with the liveliness and loveliness which was its wont in other days. The old-fashioned pharmacy has passed away, the old-fashioned pharmacist passed with it. The old-fashioned doctor whose existence largely made possible the existence of the old-fashioned apothecary has also gone the way of all things human, and into his place has stepped the natty young doctor of

to-day who frowns on pills and powders, and whose materia medica consists of ten drugs, eight of which he rarely uses, nor knows how to use.

It is not ours to commiserate over this with the dear public who suffer patiently in the interest of medical progress, because the twentieth-century doctor cannot prescribe until the laboratory designates the nine odd germs that cause the patient's distress. It may take the laboratory nine days to establish the diagnosis, and it may be that by this time the patient is on the ninth lap of the final heat; be that as it may, the diagnosis must be established—and "Presbyterianism" may come to the patient's rescue.

All of this to emphasize the fact that the old-time prescription writers are not with us, and that the new school of medicine walks on the crutches of diagnosis and lets treatment play second fiddle. So this along with many other factors has changed the entire complexion of our calling.

Prohibition opportunities, legally and otherwise, have gathered into the ranks of pharmacy men whose motives are not beyond reproach, and who are not hesitating, for the sake of financial aggrandizement, to bring the entire calling into rank disrepute. In the retail end of the practice of pharmacy the old-timers stand pat and live to the letter of the law, but they gaze in wonderment at the drug store that mushrooms into the neighborhood over night and earns for its shady proprietor "Packard" profits on a "Flivver" investment. What can we do to curb these practices? This is not advice, this is something to think about.

And again in the cities the confectioners and cigar stores are mutating over night into drug stores—drug stores without a druggist. Commercial establishments that sell anything from a pill to a pincushion—anything purchasable at a drug store except the prescription. The dear old public again is foozled. Father walks in for his mineral water, mother for her foot powder, sister for her chin varnish and brother Bob for his chew of plug entirely unaware of the fact that the establishment which they patronize thrives by misappropriating the prestige which is rightly the pharmacist's.

Medicine chases the chiropractor, the naprapath and all the other paths to easy money with a Dutch Cleanser's eagerness—because these new so-called professions are humbugs and quackeries. What shall legitimate Retail Pharmacy do with poachers and trespassers on its premises? Something else to think about.

Hospital pharmacy, and it is a pleasure to dedicate our second session to this enlarging field of our endeavors, is looming large as the one means of perpetuating our practice. Here is where the falling torch can again be thrust on high, for there is in this part of our calling a real field for professional service.

Hospital pharmacists within this Association are aiming to organize with a view to creating a section or division which shall be representative of their particular ideas and interests. As a hospital pharmacist of long standing, as a loyal member of the American Pharmaceutical Association, and as chairman of this Section, I heartily believe that such an organization can function well only if it is made part of the American Pharmaceutical Association. Just how this can be done is another question. There is existent a committee, delegated by your chairman to inquire into the matter and to present a report. So that we may not embarrass this committee we refrain at this time from making any definite recommendation.

In conclusion the thanks of the chair are due to the secretary, Mr. Becker, for his able assistance, and to the members of the Association who pledged their loyalty to the Section not by their presence alone, but also by contributing papers towards the program, which will prove, we hope, as interesting and instructive as in other years.

Respectfully submitted,

(Signed) IVOR GRIFFITH.

The report was received and referred for publication.

Chairman Griffith appointed Messrs. F. P. Stroup, W. L. Scoville and William Gray members of the Committee on Nominations.

The report of the Committee on National Formulary was read by Chairman W. L. Scoville:

REPORT OF THE NATIONAL FORMULARY COMMITTEE.

To the American Pharmaceutical Association:

The progress of the revision of the National Formulary has been very satisfactory during the past year. The revision has now reached the stage of steady detailed work, and the members

of the Committee are industriously engaged in perfecting the details. Questions of policy and principles of procedure have been established, and many of the articles have received their final sanction for the next edition. One hundred and forty preparations have been dropped, and seventy-eight have been added. Of the latter, twenty-four are articles recommended for deletion from the U. S. P. These figures refer to articles in Part I, preparations only, and do not include articles in Part II, which is composed entirely of articles needed in Part I and not recognized in the U. S. P. It is perhaps needless to say that the N. F. Committee is acting here in harmony with the U. S. P. revision, so that the two books will be consistent.

We have broken away from the former policy of recognizing every preparation that is dropped from the Pharmacopoeia. The above twenty-four preparations which are taken from the U. S. P. IX represent less than half the number of preparations which have been tentatively deleted. This is a significant change from our former custom of introducing into the Formulary every preparation which is deleted from the Pharmacopoeia. The principle of accepting preparations on the basis of usage now is applied to all articles whether from the Pharmacopoeia or from other sources.

Some of the preparations now official in the N. F. have been reclassified, notably some troches which will reappear as elixirs or as tinctures. The question of deleting the wines has been very thoroughly discussed and was twice acted upon. The right of the N. F. to continue these preparations has never been questioned, and the action has been based entirely upon a consideration of their value and uses together with practical difficulties which have arisen concerning their manufacture.

They were first deleted after a full discussion in an assembly of the committee by nearly unanimous vote. During the past year protests have been received from individuals and organizations outside the committee against the deletion of the wines. These protests have been published in the committee bulletins and have led to a motion to reconsider, which was very thoroughly discussed. The motion to reconsider was lost by a vote of 9 to 2. Thus the wines as a class are eliminated but the wines of antimony, colchicum corm, colchicum seed, and ipecac will be reformed into tinctures, and authority will be given to supply these whenever the respective wines are directed, on prescriptions or otherwise. Wine of Beef and Iron will be formulated into an elixir.

A chapter on Ampuls has been prepared, and six typical ampul solutions have been admitted. Also a short chapter on Tablets has been prepared.

The Pharmacopoeia having dropped its chapter on Diagnostic Reagents, this will be added to Part III of the N. F., after revision.

The chemical solutions will have physical descriptions as well as additional tests and assays.

The committee on Pepsin is still at work studying the conditions of stability in solutions, and the rate of deterioration. It is expected that this study will result in more stable solutions of pepsin and a better understanding of their properties.

Some correspondence has been held with manufacturing houses regarding the standard for rennin and its method of assay, which is likely to result in more satisfactory conditions with this substance.

Letters were sent to about fifty pharmaceutical manufacturers asking for data on the alcoholic strength of N. F. preparations. This resulted in a collection of data which will be of great value in establishing alcoholic standards for these preparations. The results of this correspondence were published in the July number (1922) of the JOURNAL. This subject is to be followed up further.

It should be noted that the drug manufacturers show a very cordial and generous disposition to aid in the revision even at a considerable cost to themselves.

The committee of the American Association of Veterinary Medicine which was appointed about a year ago to coöperate in the devising and revising of veterinary formulas has been enthusiastically at work. It is composed of three of the leading veterinarians and some excellent results are anticipated from its work.

The American Dental Association committee has shown little interest in the revision and little is expected from that source.

There is to be further consideration of preparations for addition to the N. F. and the following list of added preparations is to be taken as those authorized to date only. Some others

are likely to be added. The work has, however, progressed far enough to indicate that the next edition of the National Formulary will be larger, more up to date and more generally useful than any that have preceded it.

List of Preparations Added to the National Formulary.

Acid Nitrohydrochloric (U. S. P. IX)
Acid Nitrohydrochloric Diluted (U. S. P. IX)
Ampuls, Chapter on
Ampuls of Caffeine Sodio-Benzoate
Ampuls of Camphor
Ampuls of Emetine Hydrochloride
Ampuls of Quinine and Urea Hydrochloride
Ampuls of Quinine Dihydrochloride
Ampuls of Sodium Cacodylate
Citrated Caffeine (U. S. P. IX)
Collodion, Ichthyol
Diagnostic Reagents
Elixir Aletris Compound
Elixir Antiasthmatic
Elixir Beef and Iron
Elixir Buchu Juniper and Potassium Acetate
Elixir Catnip and Fennel
Elixir Creosote and Terpin Hydrate
Elixir Digestive Compound
Elixir Four Chlorides
Elixir Five Bromides
Elixir Guarana and Celery
Elixir Guarana Compound
Elixir Helonias Compound
Elixir Hydrangea and Lithia
Elixir Hydrastis Compound
Elixir Manaca and Salicylates
Elixir Saw Palmetto and Sandalwood Compound
Elixir Tonga Compound
Extract of Malt (U. S. P. IX)
Extract of Sumbul (U. S. P. IX)
Extract of Taraxacum (U. S. P. IX)
Fluidextract of Cimcifuga (U. S. P. IX)
Fluidextract of Avena Sativa
Fluidextract of Digitalis (U. S. P. IX)
Fluidextract of Frangula (U. S. P. IX)
Fluidextract of Guarana (U. S. P. IX)
Fluidextract of Sarsaparilla (U. S. P. IX)
Fluidextract of Sarsaparilla Compound (U. S. P. IX)
Fluidextract of Manaca
Fluidextract of Stillingia (U. S. P. IX)
Fluidextract of Taraxacum (U. S. P. IX)
Fluidextract of Triticum (U. S. P. IX)
Fluidextract of Viburnum Prunifolium (U. S P. IX)
Fluidextract of Xanthoxylum (U. S. P. IX)
Granular Effervescent Magnesium Sulphate
Infusion of Senna Compound (U. S. P. IX)
Lotion of Calamine
Lotion of Calamine Compound
Liniment of Calamine
Ointment Capsicum, Compound
Ointment Ichthyol
Ointment Mustard, Compound
Pencils of Iodine
Petroxylin, Ichthyol
Syrup of Calcium Lactophosphate (U. S. P. IX)
Syrup of Chocolate
Syrup of Hypophosphites (U. S. P. IX)
Syrup of Sarsaparilla, Compound (U. S. P. IX)
Syrup of Thyme
Syrup of Thyme, Compound
Syrup of Trifolium, Compound
Tablets, Chapter on
Tablets of Charcoal (replacing Troches)
Tablets of Phenolphthalein (replacing Troches)
Tablets of Quinine Tannate (replacing Troches)
Tablets of Santonin (replacing Troches)
Tablets of Santonin Compound (replacing Troches)
Tablets of Sulphur and Potassium Bitartrate (replacing Troches)
Tinctures, Type formulas for
Tincture of Antimony (replacing Wine)
Tincture of Arnica (U. S. P. IX)
Tincture of Colchicum Corm (replacing Wine)
Tincture of Colchicum Seed (replacing Wine)
Tincture of Guaiac (U. S. P. IX)
Tincture of Guaiac, Ammoniated (U. S. P. IX)
Tincture of Ipecac (replacing Wine)
Tincture of Sanguinaria (U. S. P. IX)
Troches of Red Gum

Articles Added to Part II of the National Formulary.

Ammonium Valerate (U. S. P. IX)
Anise (U. S. P. IX)
Arnica (U. S. P. IX)
Avena Sativa (U. S. P. IX)
Calcium Glycerophosphate (U. S. P. IX)
Calcium Hypophosphite (U. S. P. IX)
Cascara Amarga (?)
Chondrus (U. S. P. IX)

Cimcifuga (U. S. P. IX) (?)
Cinchonidine Sulphate (U. S. P. IX)
Coriander (U. S. P. IX)

Diacetylmorphine Hydrochloride (U. S. P. IX)

Fennel (U. S. P. IX)
Frangula (U. S. P. IX)

Guaiac Resin (U. S. P. IX)
Guarana (U. S. P. IX)

Hops (U. S. P. IX)

Ichthyol

Lithium Benzoate
Lithium Bromide (U. S. P. IX)
Lithium Carbonate (U. S. P. IX)
Lithium Citrate (U. S. P. IX)

Malt (U. S. P. IX)
Manaca
Manna (U. S. P. IX)
Matricaria (U. S. P. IX)
Mercuric Oxide, Red (U. S. P. IX)
Mezereum (U. S. P. IX)
Mitchella Repens

Oil of Pimenta (U. S. P. IX)

Potassium Hypophosphite (U. S. P. IX)

Red Gum

Sabal (U. S. P. IX)
Sanguinaria (U. S. P. IX)
Sarsaparilla (U. S. P. IX)
Sassafras (U. S. P. IX)
Sodium Arsenate, Dried (U. S. P. IX)
Sodium Glycerophosphate (U. S. P. IX)
Sodium Glycerophosphate Solution (U. S. P. IX)
Sodium Hypophosphite (U. S. P. IX)
Strychnine (U. S. P. IX)
Sumbul (U. S. P. IX)

Taraxacum (U. S. P. IX)
Tonga
Trifolium
Triticum (U. S. P. IX)

Veratrine (U. S. P. IX)
Viburnum Prunifolium (U. S. P. IX)

Xanthoxylum (U. S. P. IX)

Zinc Carbonate, Precipitated (U. S. P. IX)

Detroit, Aug. 1, 1922.

WILBUR L. SCOVILLE, *Chairman.*

L. E. Sayre asked relative to stabilizing pepsin preparations. Chairman Scoville replied that the work of the committee had not been completed.

The report was received. The reports of the Committees on U. S. Pharmacopoeia and Unofficial Formulas are printed in the October number of the JOURNAL, pp. 833 and 859.

The following papers were read and discussed:[1]

"Some Apparatus Used in the Drug Store," by Crosby B. Washburne. (See p. 703, September JOURNAL A. Ph. A.)

"Aqueous Elixir and Alcoholic Elixir *vs.* Aromatic Elixir," by Clyde M. Snow and Bernard Fantus. (The paper is to be published with discussion thereon. It was voted to refer a consideration of this paper, and bring the two elixirs to the attention of the Committee on National Formulary.)

"Some Incompatibilities of Aspirin,"[2] by E. A. Ruddiman. (See p. 796, October JOURNAL A. PH. A.)

"Infusion of Digitalis," by Caswell A. Mayo.

"Further Notes on Tincture of Cantharides," by F. W. Nitardy. (The paper was referred to Chairman George M. Beringer, U. S. P. Revision Sub-Committee No. 11.)

"Stainless Steel in the Drugstore," by F. J. Blumenschein.

"Experiments on Improving the Keeping Qualities of Chalk Mixture," by Bernard Fantus and Clyde M. Snow. (See p. 795, October JOURNAL A. PH. A.)

The following papers were read by title and referred to the Publication Committee:

"Physics in Pharmacy," by J. U. Lloyd.

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[1] Papers to be printed will hereafter be followed by discussions.

[2] During the discussion of the paper, C. J. Clayton asked whether the changes were toxic or merely physical. The author replied that he had not determined. Messrs. Gray, Griffith, Rudd, and Miss Hamilton, speaking from experience, stated that in their opinion the combination of quinine and aspirin was not toxic; references to published articles on the subject were also given.

"The Use of an Indicator in the Compounding of a Powder Prescription," by C. A. Greenstone.

"Silica Gel as a Filtering Agent in Pharmacy," by John C. Krantz, Jr.[1]

"Leeches and How to Dispense Them," by Otto Raubenheimer.

"The Permanency of Some Dyes," by E. A. Ruddiman and R. H. Clark.

"The Volatility of Chloroform from Chloroform Liniment," by J. W. E. Harrisson.

"Variance in Powdered Extracts," by E. H. Hessler.[2]

"A Few Rare Incompatibilities," by Ralph Calvert. "Medicinal Charcoal," by Ralph Calvert.[3]

The first session of the Section on Practical Pharmacy and Dispensing was then adjourned.

SECOND SESSION.

The second session of the Section on Practical Pharmacy and Dispensing was convened at 2:00 P.M., August 17, by Chairman Ivor Griffith. Reading of minutes was by motion dispensed with.

Chairman Griffith announced that the papers of this session were concerned with hospital pharmacy. The following papers were read:[4]

"Pharmacists for Small Hospitals," by Mabel Starr.

"Hospital Pharmacy," by W. H. Ford.

"The Status of the Hospital Pharmacist," by Ivor Griffith.

"Weight for Volume Solution of Potassium Iodide,"[5] by Irwin A. Becker. The paper was discussed by Messrs. Ford, Gray, Lakey, Fantus, Root, and others.

"Antiseptic Solutions," by Bruno Höckert.

The following papers were read by title and referred to the Publication Committee:

"Buying for the Hospital Pharmacy," by Frances M. Greenwalt.

"Duret's Solution in Hospital Practice," by Carl F. Dyna. (See p. 801, September JOURNAL.)

"The Hospital Pharmacist, and His Importance," by Edward Swallow.

"The Diagnosis and Treatment of Hay Fever," by Ivor Griffith. (See September JOURNAL, p. 792.)

"Testing Ink for Sterilizers and Autoclaves," by Ivor Griffith and Morris Griffith.

"Leeches: How to Dispense Them," and "Mixtum Compositum," by Otto Raubenheimer.

In discussing the paper by Pharmacist Edward Swallow, Chairman Griffith referred to a visitation by a man of authority to inquire into the management of the hospital with which he is connected. Thorough examination was made of everything in and about the hospital, except the pharmacy. The importance of the latter as part of a hospital was fully impressed upon the Commissioner, and he evidenced his appreciation of the importance. "As a result," the speaker stated, "and the coöperation of other hospital pharmacists, the hospital pharmacy will hereafter be included in the inspections of Pennsylvania hospitals."

Chairman Griffith stated that no report had been received from the committee to effect permanent affiliation of hospital pharmacists within the Association. He hoped that the plan of devoting one-half of the annual sessions to hospital pharmacy would be continued. This proved to be the consensus of opinion of those participating in the successful program.

After hearing the report of the Committee on Nominations, which stated that Secretary Irwin A. Becker declined nomination for the chairmanship of the Section, the following officers were elected: *Chairman*, Crosby B. Washburne, Detroit, Mich. *Secretary*, Robert J. Ruth, Elyria, Ohio. *Associates:* Miss Mabel Starr, Buffalo, N. Y.; Edward Swallow, New York, N. Y.

Chairman Griffith thanked the officers and members; the new officers were declared duly installed, and, on motion, the final session of the Section on Practical Pharmacy and Dispensing was adjourned.

(To be concluded.)

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[1] September JOUR. A. PH. A., p. 701.

[2] October JOUR. A. PH. A., p. 800.

[3] October JOUR. A. PH. A., p. 798.

[4] These papers will hereafter be published with discussions thereon in the JOURNAL A. PH. A.

[5] Printed in September JOUR. A. PH. A., p. 702.

THE U. S. PHARMACOPOEIA—TENTH REVISION.*

BY E. FULLERTON COOK, CHAIRMAN.

During the next few months abstracts will be published of many of the changes in descriptions and standards and new descriptions and standards, proposed for the new Pharmacopoeia, and criticism of these is invited.

This policy is in keeping with that recommended by the U. S. P. convention to insure pre-publication publicity and elimination of errors and it is hoped that they will be given wide publication in the medical and pharmaceutical press.

The publication of these abstracts indicates progress in the revision but not its completion.

ADMISSIONS AND DELETIONS.

It is possible at this time to publicly announce an additional list of admissions and also further recommendations of the Sub-committee on Scope concerning U. S. P. Ninth, titles which should not, in their judgment, be admitted to the Tenth Revision. Anyone who disagrees with these recommendations is invited to submit a statement, setting forth their reasons, supporting it if possible with convincing evidence. The Sub-committee on Scope are earnestly searching for facts to support every claim of therapeutic value, that the Pharmacopoeia may contain only dependable remedies.

Every letter or published article on this subject which has come to the attention of the chairman has been published in the official circulars and referred to the Special Referee Committee, consisting of the twenty-one physician members of the General Committee of Revision. This Committee has just organized, electing the General Chairman of the Revision Committee as its chairman, that every physician may be free to discuss and vote on the questions presented.

Additional admissions are as follows:

Aqua Camphorae
Codeinae Sulphas
Eugenol
Extractum Cannabis
Extractum Colocynthidis Compositum
Emplastrum Plumbi
Emplastrum Sinapis
Elixir Aromaticum
Extractum Glycyrrhizae
Extractum Colchici Cormi
Ferri Sulphas Granulatus
Fluidextractum Sabal
Fluidextractum Cochici Seminis
Fluidextractum Belladonnae Radicis
Fluidextractum Buchu
Fluidextractum Cannabis
Fluidextractum Eriodictyi
Fluidextractum Hyoscyami
Fluidextractum Rhois Glabrae
Fluidextractum Senegae
Gelatinum Glycerinatum
Hypophysis Sicca
Linimentum Calcis
Linimentum Camphorae
Linimentum Chloroformi
Linimentum Saponis
Linimentum Saponis Mollis
Liquor Ferri Chloridi
Liquor Ferri et Ammonii Acetatis
Liquor Hypophysis
Liquor Iodi Compositus
Massa Hydrargyri
Myristica
Phenolsulphonephthalein (diagnostic)
Pilulae Aloes
Pilulae Asafoetidae
Pilulae Ferri Carbonatis
Pulvis Glycyrrhizae Compositus
Pulvis Jalapae Compositus
Pulvis Rhei Compositus
Quininae Hydrobromidum
Resina Jalapae
Serum Antidiphthericum
Spiritus Aurantii Compositus
Syrupus Acidi Citrici
Syrupus Picis Liquidae
Syrupus Senegae
Syrupus Tolutanus
Thyroxin
Tinctura Aconiti
Tinctura Calumbae
Tinctura Gambir Composita
Tinctura Lavandulae Composita
Tinctura Kino
Tinctura Myrrhae
Tinctura Nucis Vomicae
Tinctura Opii Camphorata
Tinctura Scillae

* See also December JOUR. A. PH. A., 10, 928, 1921.

Tinctura Valerianae
Tinctura Veratri Viridis
Trochisci Acidi Tannici
Trochisci Ammonii Chloridi
Trochisci Sodii Bicarbonatis
Unguentum Diachylon
Unguentum Gallae
Veratrum Viride

U. S. P. (NINTH) TITLES NOT RECOMMENDED FOR ADMISSION TO THE U. S. P. (TENTH REVISION).

Amygdala Dulcis
Aqua Creosoti
Arnica
Cinnamonum Zeylanicum
Coriandrum
Emulsum Amygdalae
Extractum Cimcifugae
Extractum Ergotae
Extractum Gelsemii
Extractum Hydrastis
Extractum Opii
Extractum Sumbul
Extractum Physostigmatis
Extractum Taraxaci
Extractum Viburni Prunifolii
Fluidextractum Aromaticum
Fluidextractum Aspidospermatis
Fluidextractum Aurantii Amarae
Fluidextractum Cimcifugae
Fluidextractum Digitalis
Fluidextractum Eucalypti
Fluidextractum Frangulae
Fluidextractum Gelsemii
Fluidextractum Granati
Fluidextractum Grindeliae
Fluidextractum Guaranae
Fluidextractum Pilocarpi
Fluidextractum Podophylli
Fluidextractum Sarsaparillae
Fluidextractum Scillae
Fluidextractum Spigeliae
Fluidextractum Staphisagriae
Fluidextractum Stillingiae
Fluidextractum Sumbul
Fluidextractum Taraxaci
Fluidextractum Tritici
Fluidextractum Viburni Prunifolii
Fluidextractum Xanthoxyli
Gelsemium
Grindelia
Glyceritum Hydrastis
Infusum Sennae Compositum
Liquor Sodii Arsenatis
Oleum Cubebae
Sodii Cyanidum
Sodii Sulphis Exsiccatus
Spiritus Juniperi
Stillingia
Syrupus Lactucarii
Tinctura Arnicae
Tinctura Gelsemii
Tinctura Aloes
Tinctura Guaiaci
Tinctura Guaiaci Ammoniata
Tinctura Hydrastis
Tinctura Moschi
Tinctura Physostigmatis
Tinctura Pyrethri
Tinctura Quassiae
Tinctura Lactucarii
Tinctura Sanguinariae
Trituatio Eleterini
Unguentum Stramonii
Zinci Carbonas Precipitatus

There are a few questions of admission and deletion not yet announced by the Sub-committee on Scope but their final report is promised soon.

Physiological Standardization.—The U. S. P. IX made a compromise in the introduction of standardization by physiological methods. It was first proposed to require no such standards but adopt official methods for a number of the drugs and preparations and make their use optional.

This plan established uniformity for important drugs and preparations when physiologically standardized and concentrated attention upon specific process, thus making it possible to secure experience and much valuable data. Contrary to the original intention of the committee the standard for cannabis and solution of hypophysis was made compulsory. The time has come, however, for requiring physiological assay methods for other important drugs and their preparations, including digitalis, suprarenalin, ergot, cannabis, and others. To do this successfully the sub-committee recommend that an arrangement be made whereby the necessary chemicals, drugs or preparations of standard activity be made available to all manufacturers from a central station. An effort is being made to establish such a distributing center, possibly utilizing the office of the chairman of the Committee of Revision.

PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and its branches shall become the property of the Association, with the understanding that they are not to be published in any other publication than those of the Association, except by consent of the Committee on Publication."—By-Laws, Chapter X, Art. III.

Reports of the meetings of the Local Branches should be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten, with wide spaces between the lines. Care should be taken to give proper names correctly, and manuscript should be signed by the reporter. To maintain its activity and representation each branch should see that at least three of its meetings during the year are reported in the JOURNAL.

BALTIMORE.

The first monthly meeting of the Baltimore Branch of the A. Ph. A. for the season 1922–1923 was held at the Hotel Emerson on Wednesday evening, September 27, 1922.

The meeting was devoted to reports of the annual conventions. Dr. Hermann Engelhardt spoke concerning the activities of the Scientific Section of the American Pharmaceutical Association, telling of the great number of papers presented, and the many and varied subjects covered. Dr. E. F. Kelly reported on the work accomplished in the House of Delegates and in the General Sessions, pointing out how the proposed plan of reorganizing the A. Ph. A. was slightly modified and accepted by the General Session, to be later ratified by the state associations. Dr. Geo. A. Bunting was unable to attend the Branch Meeting, but sent in a report of the work accomplished in the meetings of the National Association of Boards of Pharmacy at Cleveland, which was read by the secretary. B. Olive Cole reported on the sessions of the Section on Education and Legislation, and the American Conference of Pharmaceutical Faculties, pointing out that both of these bodies stressed the need of uniformity of requirements, etc.

Dr. Neil E. Gordon and Dr. John C. Krantz, Jr., who attended some of the sessions of the semi-annual meeting of American Chemical Society in Pittsburgh, reported on the interesting happenings of those sessions; and Dr. E. F. Kelly, who was present at the opening sessions of the National Association Retail Druggists in Detroit, told of some of the things accomplished there.

Echoes from the national conventions made the evening's program most interesting, and Mr. Robert S. McKinney expressed his appreciation of the reports, and said he was well repaid for his trip of forty miles in order to attend the meeting of the Branch.

In sending out notices of the meeting, special attention was called to the fact that under the reorganization plan for the A. Ph. A. it is necessary that the Branches hold not less than six annual meetings, with an attendance of not less than fifteen members at each meeting, in order to have a representative in the House of Delegates. The A. Ph. A. members in Baltimore hope to maintain a representative Branch.

B. OLIVE COLE, *Secretary-Treasurer.*

CHICAGO.

The 128th meeting of the Chicago Branch of the American Pharmaceutical Association was held Friday evening, October 6, at the University of Illinois School of Pharmacy Building. President C. M. Snow presided. Secretary E. N. Gathercoal stated that a program for the meetings of the winter had not been completed but that a number of splendid offers were in sight. There is a good promise of some noted speakers from outside of Chicago during the winter; one meeting is to be devoted to a discussion of the latest and most promising discoveries in hospital pharmaceutical practice, and at one or two meetings original contributions from Chicago men will be presented. The secretary also stated that the membership of the Branch was now exactly 400 and that the prospects for a large increase in membership this year were good and that plans were being laid for a strong membership drive. It is hoped to see the membership reach 500 during the year.

Secretary Samuel C. Henry of the National Association Retail Druggists, who had just returned from the great convention in Detroit, presented a most able address embodying his impressions of this convention. Secretary Henry stated that the latest figure on registration he had seen was 3010. The attendance at the business sessions was very large. It was Mr. Henry's impression—not only of the Detroit convention but also of the American

Pharmaceutical Association convention at Cleveland, and of the several state conventions that he attended during the summer—that the interest of retail druggists in their organizations was manifested more than ever before and, especially, their desire to increase the power and forward the usefulness of these associations. He prophesied prosperity and better standing of the retail druggist. Dr. J. H. Beal's address at Detroit struck the keynote of conditions in American pharmacy and not alone of conditions in American pharmacy, but also the conditions in the American nation as a whole. Dr. Beal said a great danger lies in the increasing tendency of our government to regulate by autocratic decrees the business and profession of pharmacy; not alone is pharmacy affected in this respect, but so much of the business and the intimate life of the people is affected that the entire American nation has come under the hampering influence of this autocratic form of government. Secretary Henry, in a very optimistic tone, however, stated: "We are coming closer together in the great associations and forming a united front against conditions that mean disruption to pharmacy, and we should feel much gratification for the progress that has been made in this respect this year."

President S. L. Antonow of the Illinois Pharmaceutical Association, in a very able talk, presented some of the outstanding features of the state association meeting at Springfield last June. The state association meeting was a splendid convention of the druggists of the state, with perhaps the largest attendance and one of the best programs. He further stated that the state association had promise of an exceptionally strong legislative committee this year and that a great effort would be made to carry out the legislative resolutions adopted at the convention. He made special reference to the resolution so unanimously carried which restricts the sale of all medicinal preparations containing more than $^1/_2$ percent of alcohol to the supervision of a registered pharmacist. President Antonow also referred to the A. Ph. A. Convention at Cleveland which he pronounced one of the most successful that he had ever attended. He eulogized the splendid work of Dr. H. V. Arny and mentioned his nomination for the presidency.

General Secretary W. B. Day spoke of the very successful A. Ph. A. Convention in Cleveland. This convention was a success from every standpoint. The attendance was large, the papers read were numerous and instructive and the entertainment was most generous. He discussed the reorganization plan and explained that while giving more power to the House of Delegates the plan in no sense took away from the members of the Association their control of the organization. Surprise had been expressed at the appearance of the entire Executive Committee of the N. A. R. D. at the A. Ph. A. Convention and a few had feared that it was the forerunner of absorption of the A. Ph. A. by the N. A. R. D.—a fear that was entirely groundless. On the contrary, the developments of the convention at Cleveland will bring the two national organizations into closer coördination and will redound to the great benefit of pharmacy. The N. A. R. D. occupies the special field in looking after the business and legislative interests of the retail druggists. The A. Ph. A. occupies a no less important field in caring for their professional welfare and their scientific advancement. The A. Ph. A. alone of all national organizations is in a position to speak for pharmacy as a whole, for in it are represented not only the retail druggists but all others who are interested in pharmacy from any standpoint. Professor Day also referred to the newly formed group of hospital pharmacists and the fact that their prospects were bright and that many hospital pharmacists were affiliating with the organization. He prophesied an increased usefulness for this new group. The outlook for pharmacy and for the A. Ph. A. is bright.

E. N. GATHERCOAL, *Secretary.*

CINCINNATI.

The Cincinnati Branch of the American Pharmaceutical Association held its monthly meeting at the Lloyd Library, October 10. The principal speaker of the evening was Dr. Frank B. Cain, his subject was:

THE MERITS OF A PHARMACEUTICAL EDUCATION.

The fact that pharmacists were not sufficiently organized to receive the proper recognition in the late war with Germany is much to be deplored. France and other countries recognized the pharmacist and placed him at his professional work in the army to secure the maximum efficiency. The American pharmacist felt that it was good to serve Uncle Sam in any case, but that it would be much better to serve most efficiently in his chosen line of work.

I believe the only remedy to bring about a better recognition of the worthy pharmacist,

is to educate the public to the great need of the work done by the pharmacist—to impress on the public the value of the service performed by the pharmacist in supplying medicines prepared by skilled and educated dispensers accustomed to the work, and who, by concentrating attention on the specific task of accurate dispensing, relieves the doctor of much labor, permitting him to give his whole attention to the study of diseases.

It must not be forgotten that the pharmacist who prepares medicine, like the doctor who prescribes it, must also be specially educated. Every state in the Union requires by law that anyone who fills prescriptions must first pass a state board of pharmacy examination, and then boards require two to four years' special training before the candidate is eligible for examination.

I believe that the higher prerequisites now being required for entrance to a college of pharmacy truly merit recognition by our standard universities. It is my opinion that the first two years of a pharmacy course in a recognized college of pharmacy, giving six hundred hours of work each year as outlined by the new Ohio pharmacy law, should be recognized as the equivalent of units in similar branches, especially if this work is done under the supervision of a university.

I believe that the two years spent in a college of pharmacy to obtain the degree of graduate in pharmacy should be recognized as the equivalent of the two years pre-medical work required for admission to the medical department, it being understood that a recognized high school diploma was required for entrance to the pharmacy department.*

I believe that such recognition would be in the interest of the public welfare, and I will go so far as to say that if all candidates for admission to medical schools were required to have a college of pharmacy diploma or the equivalent of work in the university, the graduate of medicine of the future would be as well if not better qualified to serve the public than they now are.

Dr. S. P. Cramer, a Cincinnati physician, gave a very interesting account of the economic conditions existing in Great Britain and in Germany, where he spent some months last summer, and spoke of the disastrous effect of the decline in the value of marks on the cultured classes in Germany.

The university professors are receiving nominally the same salary but are receiving in dollars less than one per cent of their former salary. Since the prime necessities of life have to be paid for in dollars they are in a very bad way. Every professor has been compelled to undertake some additional work in order to keep body and soul together. The situation appears almost hopeless. The fee which a dentist charged for extracting a tooth was two cents American money or ten marks in German money.

The wealthy who had fixed incomes dependent upon the income from real estate suffer a great deal because they have not been permitted to increase the rentals in a ratio sufficient to compensate for the decline in marks. Berlin, one of the greatest of cities, now looks shabby and dilapidated.

Dr. Caswell A. Mayo gave a special lecture before the students of the Medical School of the University of Cincinnati on Monday afternoon, October 9th, on the physical aspects of the colleges of pharmacy of the United States. The lecture was illustrated by over 200 lantern slides, showing the physical aspects of the colleges. Dr. Mayo said that over $20,000,000 were invested in the buildings and equipment devoted to the teaching of pharmacy.

NEW YORK.

The October 1922 meeting of the New York Branch of the American Pharmaceutical Association was called to order in the New York Colleg of Pharmacy Building, October 9, at 8:15 P.M., with President C. P. Wimmer in the chair.

Thirty-four members and friends were present.

The minutes of the preceding meeting were read and approved.

Audit Committee.—Dr. Diner reported all bills paid.

Treasurer's Report.—Dr. Horstman brought in a written report which was ordered filed.

Education and Legislation.—Mr. Eddy brought in a report which consisted principally of a discussion of the various narcotic bills now being considered.

It was moved, seconded and carried that the New York Branch go on record as opposing any model state narcotic legislation, pending a fair-minded and unbiased investigation.

Council.—Dr. Jacob Diner, Chairman of the Committee to represent our Branch on the

* The suggestion advanced was endorsed by the Branch and the paper referred to the Editor of the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION for publication.

Academy of Pharmacy Committee reported on the work done by this Committee during the summer.

It was moved, seconded and carried that the New York Branch request that the state pharmaceutical association have a Bill introduced requiring that the ownership of drug stores be limited to registered pharmacists.

REPORTS OF DELEGATES TO THE CONVENTIONS.

Dr. C. P. Wimmer announced that because of the various interests covered at the A. Ph. A. meeting in Cleveland he had divided the work of reporting this convention among several of our members:

Professor Hostmann reported on the House of Delegates; Professor Arny on the Council and general meetings of the A. Ph. A.; Professor Diekman on the National Association of Board of Pharmacy, and Professor Schaefer on Entertainments. Dr. Joseph L. Mayer reported on the New York State Association Meeting; Chas. W. Holton on the New Jersey State Pharmaceutical Association; Professor C. P. Wimmer on the Connecticut Meeting; and Clyde L. Eddy on the Convention of the National Association of Retail Druggists.

SCIENTIFIC SECTION.

Dr. Diekman, Chairman of the Committee on Progress of Pharmacy announced, in view of his having prepared a report on the work of the N. A. B. P., he would forego reading his Progress of Pharmacy Report.

Dr. Jacob Diner read a very interesting paper on "The Use and Abuse of Drugs—from the Standpoint of the Physician."

Considerable discussion followed the reading of this report.

HUGO H. SCHAEFER, *Secretary.*

PHILADELPHIA.

The first meeting of the season of the Philadelphia Branch was held October 10th, at the Philadelphia College of Pharmacy and Science.

President Jenkins introduced the speaker of the evening, Mr. Ivor Griffith, and announced that the topic would be "Hospital Pharmacy."

Mr. Griffith read several opinions on the practice of hospital pharmacy. Some of the reports advocated the training of all pharmacy students for a period in the hospital pharmacy. They also pointed out the varied experience the hospital pharmacist obtains and the possibilities of becoming interested in other lines of endeavor through his associations. Clinical chemistry and X-ray work were particularily emphasized as presenting opportunities.

The speaker cited some of his own experiences while acting as pharmacist to the Stetson Hospital. He attributed his gradual entrance into clinical chemistry directly to his associations in the hospital work.

Cognizance was also taken of the limitations that are imposed upon those employed as pharmacists in the larger institution where little time is afforded for any other than routine pharmaceutical duties.

Miss White of the University of Pennsylvania Hospital, Mr. McNeary of the Polyclinic, Mr. Worthington of Jefferson, Mr. Borneman of Hahnemann and Mr. Thum of Lankenau were present, and all participated in the discussion opened by Mr. Thum. Mr. Thum agreed with the speaker relative to the opportunities that were afforded to the pharmacist in one of the smaller institutions. He presented a rather lengthy list of the preparations that they had prepared during the year in Lankenau Hospital Pharmacy. A few of these will suffice to show that he and his assistants are busily occupied.—525,000 mils of elixirs, 210,000 mils of emulsions, 3,700,000 mils of mixtures, 4,400,000 mils of liquid soap, 500,000 mils of solutions, 265,000 mils of tinctures, 250,000 tablets. Many other preparations were enumerated, and, in addition to these, 11,000 out-patient prescriptions were filled and 63,000 containers of medicine were furnished to the hospital patients.

Following the interesting discussions a motion was made to appoint a committee to look into the advisability of forming a Section on Hospital Pharmacy to be connected with the Local Branch. The motion carried and the appointment of the committee was left to the president.

One new member was received—Mr. Harry F. Simons, Jr.

"Legislation" will be the topic of the November meeting.

J. W. E. HARRISSON, *Secretary.*

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Compiled by A. G. DuMez, Reporter on the Progress of Pharmacy.

Under the above heading, there will appear each month a list of references to the recently published articles on pharmaceutical research.

All articles recorded in these lists will be presented in abstract form in the bound volumes of the YEAR BOOK, which is issued annually. Those desiring abstracts immediately can obtain them for a fee of one dollar each by communicating with A. G. DuMez, Hygienic Laboratory, U. S. P. H. S., 25th & E Sts., Washington, D. C.

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Rec. trav. chim., 41 (Aug. 1922), 509

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Bull. soc. pharm. Bordeaux, 60, No. 5 (1922), 124

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J. pharm. chim., 26 (Sept. 1922), 161

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CHRISTMAS SEAL SALE FUNDS.

One billion Christmas seals have been ordered for this year's sale. Eight elements toward which seal sale funds have been and are applied, are: (1) for increasing the number of hospitals and sanatoriums for the treatment of tuberculosis from 100 (sixteen years ago) to nearly 700 with approximately 60,000 beds; (2) for establishing over 550 clinics and dispensaries; (3) in securing at least 3500 special tuberculosis nurses who instruct in the home, mothers and their families; (4) toward research work; (5) for statistical study; (6) for publicity in distributing during the past sixteen years approximately 1,000,000 pieces of printed matter; (7) for the Modern Health Crusade which has enrolled nearly 8,000,000 school children; (8) toward securing over 3000 open-air schools, summer camps and preventoria.

COUNCIL BUSINESS

A. PH. A. COUNCIL LETTER NO. 3.
(Abstract.)

WASHINGTON, D. C., October 17, 1922.

To the Members of the Council:

10. H. M. Whelpley has been elected member of the Publication Committee (Items 3 and 6).

11. Nominations for member of the Committee on Research (Item 7). The following names have been placed in nomination for member of the Committee on Research: Dr. Jacob Diner by Clyde L. Eddy; Dr. Arno Viehoever by A. G. DuMez.

Since the call for nominations was sent out nearly a month ago, a vote is being called for at this time.

12. Donation of a set of Proceedings and Year Books of the Association to the Pharmaceutical Institute of the University of Dorpat. Approved.

13. Applicants Nos. 1–16 elected to active membership.

14. Deletion of wines from the N. F.—Resolutions of the Ohio State Pharmaceutical Association. The following set of resolutions has been received from the Secretary of the Council of the Ohio State Pharmaceutical Association, and is here presented for such action as the Council of the A. Ph. A. may see fit to take.

COLUMBUS, OHIO, August 30, 1922.

Resolution submitted to the Council A. Ph. A.

"WHEREAS the Committee on National Formulary of the American Pharmaceutical Association after due consideration has seen fit to delete Wines and Sherry Wine from the next (5th) edition of the National Formulary, and

"WHEREAS such deletion means in Ohio on account of the State Law Enactment that a retail pharmacist will be unable to purchase, use or sell Wines or Sherry Wine,

"*Therefore Be It Resolved* that we, the members of Council of the Ohio State Pharmaceutical Association, do petition the Council of the American Pharmaceutical Association to reconsider its action in adopting the report of said Committee in reference to deleting Wine or other listed intoxicating liquors on the following grounds:

"1. That said Committee, composed of one doctor, six retail druggists and nine teachers of pharmacy (none of whom are residents of Ohio), is not a representative committee of the retail trade;

"2. That the vote of nine for deletion and two for retention of Wines and Sherry Wine is not a representative vote;

"3. That the adoption of said report by the Section on Practical Pharmacy and Dispensing of the A. Ph. A. to which Section the Council of the A. Ph. A. had referred this report is not a proper place for the disposal of the report of this Committee on account of the legal question involved, and

"That the legal question involved is an amendment to the McCoy Ohio Prohibition Law in which certain listed preparations in the U. S. P. and the N. F. are declared to be intoxicating but which are permitted to be used and sold as medicines and as Sherry Wine is declared to be one of these listed preparations just as Aromatic Elixir or any other of the 23 listed preparations hence by the adoption of said Committee report of deletion of any of these preparations then such preparations are prohibited from being used or sold in Ohio and

"*Therefore Be It Resolved* that the retail pharmacists and the practicing physicians of Ohio be advised of such action and that we protest against the adoption of said report by the American Pharmaceutical Association and ask that the matter be reconsidered by the Council and a time set for the hearing of such an important matter.

"*Be It Further Resolved* that copy of this resolution be forwarded to the members of Council of the A. Ph. A. to the members of the Formulary Committee and to the Pharmaceutical Press. Respectfully submitted,

H. M. Highfield,
Frank Schwilk,
Harry G. Schmuelling.

Signed the members of Council
L. W. Funk,
J. W. Dysle,
Charles E. Roseman,
E. H. Thiesing,
W. L. Whelton,
Theo. D. Wetterstroem,
Secretary."

15. Request that date of next annual meeting be decided upon. Under date of October 9, 1922, Local Secretary Beard writes from Chapel Hill, N. C., as follows:

"After canvassing the situation in Asheville it seems clear that the date for the next annual meeting of the American Pharmaceutical Association should be the week beginning September third. Will you kindly take the question up with the Council so that the time may be fixed?"

A motion to comply with the wishes of the Local Secretary in this matter would appear to be in order. A. G. DUMEZ, *Secretary.*

(*To be continued.*)

THE DEPARTMENT OF THE AMERICAN CONFERENCE OF PHARMACEUTICAL FACULTIES

[EDITOR'S NOTE.—The Honorable Newton D. Baker, ex-Secretary of War, was invited to address the American Conference of Pharmaceutical Faculties at the Cleveland meeting. He gave one of the most inspiring addresses ever delivered before that body and the appeal which he makes for pharmacists to recognize the dignity of their relation to all education is most timely.

The National Association of Boards of Pharmacy was given a special invitation by the Conference to listen to Mr. Baker's address. This they did in a body and the prolonged applause which Mr. Baker received at the close of his address was only a small indication of the appreciation by his hearers of the wisdom of what he said.

The Chairman of the Executive Committee wishes to announce that the School of Pharmacy of the Agricultural College of North Dakota has been elected to Conference membership. The recent vote taken by mail at the order of the Conference was unanimous.

RUFUS A. LYMAN, *Chairman, Executive Committee and Conference Editor.*]

ADDRESS BEFORE THE AMERICAN CONFERENCE OF PHARMACEUTICAL FACULTIES AT THE 23RD ANNUAL MEETING IN CLEVELAND BY HONORABLE NEWTON D. BAKER, EX-SECRETARY OF WAR.

Ladies and Gentlemen: I assure you that I recognize myself with great difficulty when introduced as a prominent educator. I have attempted to educate but one man, and sometimes, when in recent years my duties have been so distracting, I have of necessity abandoned the course of reading in which I delighted in my youth. I have felt that my education is in a backward direction, and if I continue as I have been going for the last ten years, I will be illiterate. Yet I can say, by way of amplification, that in my experience I have had some educational contacts of an extremely interesting kind.

The one that delights me most is the greatest educational fact that ever took place in the history of mankind. When the war was over and we had something like two million men in France, it was perfectly clear that a long time would necessarily elapse before those two million soldiers could be returned to the United States. They had been taken over with the aid of the British passenger ships at a rate which, in July of 1918, reached three hundred and thirty-four thousand in a single month. But as soon as the war was over, the British needed their ships to carry their Canadian soldiers home, and their men to outlying possessions, and as many of the British were of necessity withdrawn it looked as though it would take a year to get our army home.

The question arose as to what we should do with two million men in a foreign country, with nothing to do. An army is all right while it is being formed and trained, because it has rigid and exacting duties ahead of it, and every man's attention can be centered upon the perilous things he is to encounter and the tasks he is to perform, and he realizes the necessity of preparation that he may do these things as safely as possible. But when the war is over, an army of almost any size is a danger, not only to itself, but to the country in which it happens to be, because of all the trades and occupations, that of a soldier is least compatible with idleness.

My military associates on the other side conceived the notion that the only way to keep that army from running amuck or losing its mind was to drill it all the time. They woke those boys up at five in the morning and drilled them until they fell from exhaustion. Then they would let them sleep a little while and then drill them again, and they kept that up until there was almost a riot. I think there would have been a mutiny if they had been long subjected to that process.

We were hunting for something for them to do. The suggestion was made that they might turn their home talents into the reconstruction of devastated France, but they were in no mood to build roads or houses. Their idea was that others had been responsible for the destruction. We put our ear to the ground to see what the boys themselves thought they would like to do, and I think it is a tribute to American institutions to say that the answer which came, came from the boys themselves. It was not imposed by us older people upon them, but it came from the soldiers. They said, "We want education. We have been over here a year now, and we are likely to be here a year longer. Two years have been taken out of our training for life and we want education."

We instantly set about devising an educational system for those two million men. I shall not undertake to give you the details of that operation. It was, of course, the greatest educational opportunity ever undertaken in the history of the world—suddenly, out of nothing, to provide educational facilities for two million men in a foreign country. It had to be an education that was worth something, in view of the fact that it was for mature men—men in all degrees and grades of intellectual advancement. Some of the men were unable to read and some of them had been interrupted in their courses in college, where they were pursuing highly specialized courses.

The British and French opened all their universities to our students and we filled them with about twenty thousand students without making an appreciable dent in our problem. We even sent them to Ireland, to the University of Dublin. Every university and college in France—even those that had been closed—were opened. All the universities and minor colleges of England were filled to overflowing and still we had taken only twenty thousand out of our two million. Then we set up in every division, and practically in every regiment, schools which were taught by the men themselves. They, of course, taught reading and writing to the illiterate. They taught more advanced things as far as they could, but we realized that this was not responding fully to the need.

We took a great hospital which had been built in anticipation of a great battle which we were to fight, but never fought. We had estimated that our injured and wounded in that great battle would require accommodations for something like fifteen thousand wounded men, and we had the hospital all ready for those men when they should be wounded, but when the armistice was signed, there stood the hospital. In six weeks we had a university for twelve thousand students—not an elementary or primary school, but a university.

Mathematics, chemistry, zoölogy, all the languages, biology, history, art, painting, sculpture, music, theology, law, medicine and practically every faculty that is now in the curriculum of modern universities were represented there, and we had something over twelve thousand men taking university courses of such a grade that when they came back to this country the work would fit in with the course in any university as so much time gained. The amazing part of it is that practically all the teaching in that university was done by the soldiers themselves. We often talk about militarism as though it established a caste. It does. When an army is in the field there must be subordination. There come moments when someone in command must say to those over whom he is placed, "Go and do," and there is no time for debate and no time for question or explanation. If there is to be safety at all, it must lie in instant and unquestioning obedience. No other rule is possible, and yet, when we set up this university, I had the pleasure of going through it, and in one room, as a sample, I saw an instructor with a class of twelve, teaching integral calculus. Among the students there was one major, several captains and I think all the rest were lieutenants except the instructor. He was a private.

So constituted are Americans, that a man steps from the most subordinate position to a position of command, when the order of the day is changed, and in that university we had a complete reversal of the hierarchy of command, because, on the field, the major was the highest man and the private was the lowest, but when they got into the realm of intellectual attainments, the private was in command because of his superior knowledge. Even then we found we had not really solved the problem.

We found there were men scattered all over Europe in the Army of Occupation who were too far advanced for the schools possible to be set up there, and who could not be spared to come down to the university. They were not getting what they needed in an intellectual way, so a correspondence school was set up and notices were sent to every military camp in Europe that if there was any soldier there who could not get what he wanted, and could not be spared to come to the university, if he would write to the university, it would undertake to teach him by correspondence anything he wanted to know. There was no limit to the invitation.

So the system of correspondence instruction was started with forty thousand men, and by correspondence we taught Hebrew, Greek, Latin. My impression is that we even taught German to students who had just finished a great war against the German people, and who might be thought to have some prejudice against them.

Mr. President, while I can hardly claim to be an educator at all, I do claim contact with this great educational experience, and I am taking your time to tell you that, although its seems very remote. In the first place, I think it is a great fact, a fact which every American ought to

know, that when our army was over there and we were largely in despair about what to do with them —how to entertain them, and how to occupy them—our own men solved that problem. The wisdom came from the bottom up, and not from the top down. They said, "We want education."

The second reason I tell you is because it developed a new theory and a new system of education. It was the first time, so far as any knowledge goes, in which an educational system had ever been built for adults. All other educational systems are based on the theory that children begin with the A B C's but apart from the schools which we set up in this country for teaching English and Americanization to foreign people, who usually are literate in their own tongue, I know of no other educational system which has been suddenly built for the application of grades to adult persons.

Now this brought about a new technique. We found we could not get adult persons to use the spelling books and the reading books and the arithmetic books which we use for children of six, seven and eight years of age. The whole scheme was too immature and the rate of progress was far too slow for these men, whose minds were not trained, but were simply retarded by their failure of access to opportunities, and so we had to write an entirely new system of textbooks, and to adopt a new theory of pedagogy.

The most interesting of all those experiments grew out of the suggestion of a man who said, "These men have taught us they want education; now let's let them teach us what kind of education they want." He got a group of ill-assorted men and took them into a room and said, "Now, fellows, I have been sent here to teach you political economy. I don't suppose there is one here that knows what it is, but as I am going to teach it to you—it is the science of government. After a while we will get some of its special applications, but now I want you to work out a system by which you can learn the science of government, and I am going to follow your lead. I am supposed to have more knowledge, but you are supposed to have more curiosity. My theory of education is that it is most successful when the application of knowledge is to satisfy curiosity." I think that is a very great definition.

So he said, "What do you want to know?" Nobody wanted to know anything particularly. They were more or less indifferent, but he teased them to answer a series of questions. He picked out a boy and said, "What did you notice as you came over here this morning?" He thought he would be rather funny and said he noticed that the fellows hadn't policed their kitchen very well. "Fine," said the instructor, "that is a splendid start. Whose job is it to do that?" They debated that and decided it was the job of the kitchen police. The instructor then asked, "How do men get to be kitchen police, and what happens if they do not police their kitchen?" They went through the whole scheme. They described how, if the work was not properly done, the doctor had to come around and then special officers were put in charge and exercised their authority and, beginning with that mustard seed of inquiry, he built up the great structure of government, beginning where this small and unpleasant sanitary duty was imposed on man by way of punishment, and yet representing one of the great functions of organized society, and following it through to the whole scheme of governmental organization.

Now that suggestion was so revealing that when we came back to this country—got the army back and resorted to the peace-time army—we undertook to set up, in the army schools, the theory that men who enlisted in peace time ought to be so educated that after one or two terms of enlistment they could go into civil life and not bat around as the ancient soldiers used to do. The whole army educational system is based on that system, or theory, and if you are interested in its technique you will be instructed by a visit to some army school or some library where the books that were devised for that purpose are collected and see how, out of that single man's inspiration in France, grew this remarkable development. I would not recommend it for general application, but for adult persons.

Having justified my illustration, I want to make one or two observations. There used to be a time in human affairs when it was possible for a man to know everything. There are some half-dozen names in the history of learning of men who boldly said they knew everything there was to know, and probably said it truthfully, or nearly so. The admirable Crichton was regarded as admirable because, although a youth, he ventured to post a notice on every university that if anyone wanted to debate any subject, he was ready.

Pico Giovanni, Count of Mirandela, at the age of nineteen, went from one end of the country to the other, inquiring if there were any universities around, and as soon as anyone showed

him one, he would go up and nail on the door forty-nine propositions, any one of which he was ready to debate, and these forty-nine propositions practically covered the realm of knowledge.

Leibnitz, I suppose, really knew everything, or more than any other man that ever lived, though he himself made no boast about it—he was a modest man. It was thought that Leibnitz knew all there was to know on practically every subject. Undoubtedly, Bacon knew pretty much everything. Going farther back, Aristotle knew everything in his time, but that day is now dead. It is not possible for anyone to know everything. If you took a representative body of all the greatest scientists and had five hundred men, each of whom was the most accomplished on his subject, and took them into a room, someone on the outside would invent something that they had not heard of before they went into the room.

The development of knowledge, like everything else in this world, as far as a time basis is concerned, is practically instantaneous. We have annihilated time and space. I am not talking about Professor Einstein when I say this, but we have practically annihilated space and time. If it were of the slightest importance to the President of North China Republic to know what I am saying at this moment, it would cause him no inconvenience to discover it. He would simply connect up the necessary device to hear it by radio. Within the memory of the members of this company it would have taken some months to get the information over to the President of China; we have so brought up the general level of human intelligence that all over the world there are popping up investigators, research specialists and scientifically gifted persons who are adding to the sum of knowledge at a prodigious rate. Whether we like or do not like modern education, matters little.

We can only pick out a certain limited number of fields in which we can have a fairly thoroughgoing education. Now that brings up this problem: Young men and young women come to you to be educated in a specialty. Obviously, so far as that specialty is concerned, it is of the highest importance that that educational subject should be soundly given. But if you educated them into perfect pharmacists and left off there, so that they had no contact outside of the narrow circle of the science in which you instruct them, they would not yet be equipped for life, and so the duty upon you as educators is to find out where the most fruitful contacts are between a well-given pharmaceutical education and the rest of the education which is necessary for a rounded and useful and, therefore, happy life, like on the part of those who are the graduates of your institutions.

After all, the hardest problem that a man has when he leaves college is to fit his diploma to life—it doesn't fit automatically. He gets out and life is rectangular and his diploma is round, or his diploma is rectangular and life is round. The process of fitting that diploma to life is probably the most critical and discouraging experience the young have. You can make it easier to fit the diploma if, instead of having your pharmaceutical education a round education, you have it with antennae (so to speak)—arms that reach out and touch with sympathy the related branches of learning, and that is especially interesting to pharmacists because, after all, pharmacy is a kind of half-way house between research of pure chemistry and the application of chemistry by the medical profession.

You are just in the middle—the research man discovers and the engineer carries it into practice, but the pharmacist is mid-way between those two, and if your students could have a real, live sympathy with the scientific problems of pharmaceutical chemistry and some sort of sympathetic understanding of the problems which the internal medicine doctor has to deal with—if he could see his own problems in those two points of view he would be a more useful pharmacist.

In addition to that, the pharmacist has to be a citizen. Lawyers and doctors have to be citizens and you can't be a good citizen by being merely a good lawyer or merely a good pharmacist. Sometimes I think the pharmacist has a special obligation as a citizen. He usually has his store on the corner and it is a place where the neighborhood gathers. If he is a man of firmness of character and knowledge he gets to be a man of influence quite without knowing it, because he is in the center of a village community. This is of the highest importance that, among the subjects with which you seek to inspire your students, shall be those great public subjects—political questions, if you please—in which the common good is to be worked out by coöperation of citizens.

Of course, I may add to that one other thing. There is probably no other profession in which the ethical content is so necessarily high as it is in the pharmacist's profession. For a

variety of reasons, which you will understand without my enumerating them, the druggist has control of a great set of agents which the weak and frail members of society seek to acquire for misuse, and unless the pharmacist is a man who has a very high moral purpose, unless he can see straight and think clear, he is likely to be a danger to himself and his community.

I have said all that I came here to say. What I came here to plead for was that the American Conference of Pharmaceutical Faculties should recognize the dignity of their relation to all education, for in this selective age, when it is no longer possible to know everything, the force of circumstances requires that a certain number of young men and young women shall bring their natural endowments to you to be trained. If you give them merely a limited perspective and unsympathetic education and unenlightened skill, then you have not done your whole duty by that priceless thing which those young people have brought to you to be trained, but if you give them contact with liberal and enlightening things and if you give them sympathies of a broad and general character, if you infect them with the consciousness of the fact that they are citizens and have great duties in that regard, and if you underlay all of those faculties with a broad ethical and moral basis, showing that character, after all, is the rock upon which both success and usefulness must be established, then pharmaceutical education will assume and maintain the same dignity in the great collection of educational faculties which are sought for and attained by other sciences.

NATIONAL WHOLESALE DRUGGISTS' ASSOCIATION.

In accordance with action taken at the forty-eighth annual meeting of the National Wholesale Druggists' Association, this organization will undertake a standardization of expense accounting in coöperation with the Harvard University Bureau of Business Research.

A definite plan of coöperation with the federal authorities in relation to prohibition enforcement problems with particular respect to the trade features of that law was outlined in a series of resolutions adopted in connection with the recommendations of President F. C. Groover. The association recommends the immediate segregation of the supervision of alcohol for medical purposes from the unit having charge of prosecuting violations of the law against beverage uses of liquors. It was suggested that the Commissioner of Internal Revenue appoint a deputy commissioner to perform these functions for the bureau.

Other resolutions follow:

That the Commissioner of Internal Revenue be requested to appoint an advisory trade committee from the membership of National Associations in trades employing alcohol to include the Washington representatives of such associations for purposes of consultation respecting the advisability and necessity of proposed regulations of importance to the alcohol using trades.

That The National Wholesale Druggists' Association earnestly protests against the enactment of the so-called Ernst-Wood bill removing the Prohibition Commissioner from the jurisdiction of the Commissioner of Internal Revenue, and the Secretary of the Treasury.

That The National Wholesale Druggists' Association earnestly urges the Commissioner of Internal Revenue to amend the existing office rules of the permit division in the following particulars:

"(*a*) By raising the $25,000 stock requirement of a wholesale druggist who was not in business before the National Prohibition Act went into effect to $100,000.

"(*b*) By refusing to renew permits to any applicant for a wholesale druggist's permit who employs a systematic policy of selling standard merchandise at approximate cost, as shown by advertisements, circulars, etc., thus using the wholesale drug business as a cloak to sell liquor."

In adopting the report of the Committee on Legislation the wholesale drug trade, as represented by the association membership, endorsed the suggestion that the enforcement of the Federal narcotic law be transferred from the prohibition unit to the miscellaneous division of the Internal Revenue Bureau and that the smuggling features of the law be handled by the customs division of the Treasury Department as was the case formerly.

The following were elected officers for the ensuing year: *President*, F. E. Bogart, Detroit; *Vice-Presidents*, R. H. Davis, Denver; A. B. Stewart, Seattle; W. N. Churchill, Burlington; H. D. Cowan, Buffalo; E. H. DeMoss, Louisville. New members of the Board of Control are B. B. Gilmer, Houston; A. H. Van Gorder, Cleveland; C. M. Kline, Philadelphia. C. F. Michaels, San Francisco, was made chairman of the Board of Control.

Cleveland was selected as the next meeting place.

EDITORIAL NOTES

Editor: E. G. EBERLE, Bourse Building, Philadelphia, Pa.

Committee on Publication: A. G. DUMEZ, *Chairman;* S. L. HILTON, H. M. WHELPLEY, R. A. LYMAN, W. L. SCOVILLE, and the Editor-in-Chief of the JOURNAL, General Secretary, Treasurer and Reporter on the Progress of Pharmacy, *ex-officio.*

Collaborators: JULIUS A. KOCH, President, A. Ph. A.; CHAS. H. LAWALL, President, A. C. P. F.; EDWARD WALSDORF, President, N. A. B. P.; E. FULLERTON COOK, Chairman, U. S. P. Revision Committee; S. L. HILTON, Chairman, Council A. Ph. A. The Chairmen of the Sections, A. Ph. A.: ARNO VIEHOEVER, CROSBY B. WASHBURNE, W. F. GIDLEY, WALTER M. CHASE, CLYDE L. EDDY; E. F. KELLY and WILLIAM B. DAY of the House of Delegates; A. G. DUMEZ, Secretary of the Council, the General Secretary, and the Reporter on the Progress of Pharmacy.

"HIGH-BROW STUFF" AND THE PRESCRIPTION COUNTER.

Under above caption in the *Bulletin of Pharmacy* for October, W. L. Scoville discusses the following prescription:

Solution of potassium citrate.....4 fluidounces.
Citrated caffein,
Urotropin,
Potassium acetate, of each.....2 drachms.
Peppermint water.....2 fluidounces.

Directions: A teaspoonful every 3 hours.

The author refers to articles which appeared in at least three pharmaceutical journals—and in one of the journals two different articles—on the subject of the hydrogen-ion concentration of solutions. "All of the writers," states the author, "were astute enough to suspect that this subject is of but little if any interest to the average pharmacist, and quasi-apologies therefore accompanied the papers." Professor Scoville comments further: "Thus far nobody has had the temerity to suggest that this high-brow stuff might be dragged down to the prescription counter and made to function on a guileless mixture. Wherein the sapient writers referred to in the opening paragraph missed a point." The pharmacist dispensed a clear solution, but, after standing for a while, the solution changed to a crystalline mass. An interesting explanation follows. An analysis of the reactions is given in part in the following paragraph:

"So again we consider. We now remember that potassium citrate and potassium acetate are excellent 'buffer salts.' They hinder acids or alkalies, particularly weak ones, from dissociating and, therefore, from reacting. That is to say, the urotropin has two protectors present—potassium citrate and potassium acetate—which prevent the citric acid from attacking it. So it remains calm and serene in the presence of its would-be destroyer. For the same reason the citric acid is unable to exert it solvent action on the caffeine, and the latter behaves as though it were not present."

More solvent is the answer; however, the prescription afforded an opportunity for a most interesting article.

C. P. GLADDING.

Curtis P. Gladding, recently elected president of the National Association of Retail Druggists, is a member of the American Pharmaceutical Association. He affiliated in 1912. Mr. Gladding is president of the Gladding Drug Company, of Hartford, Conn. He has been quite closely identified with local and state associations. He was a member of the Connecticut State Board of Pharmacy for two terms, and is an ex-president of Connecti-

cut State Pharmaceutical Association; for years he has been on state and national legislative committees.

A testimonial dinner was given at Hotel Garde, Hartford, October 18, which was attended by more than 200 guests from Hartford, Connecticut, and other sections of New England. Among the speakers were the Rev. Herbert Judson White, pastor of the First Baptist Church in which Mr. Gladding is a deacon; Timothy F. Shea, president of the Massachusetts Pharmaceutical Association; E. F. Gyde, president of the Connecticut Pharmaceutical Association; Samuel C. Henry, secretary of the National Association of Retail Druggists; James F. Finneran, of Boston, a former president of the N. A. R. D.; P. J. Garvin, secretary of the Connecticut Pharmaceutical Association; Colonel John W. Lowe, of Massachusetts, first treasurer of the N. A. R. D., and J. D. Hartigan, of Bridgeport, Conn., all of whom spoke of the guest of the evening in words of highest praise and esteem, pledging their support to his administration.

Oliver Franklin Fuller celebrated his 93rd birthday on October 19th, at home. Members of the Chicago Veteran Druggists' Association called in a body to congratulate their honorary president and veteran member, and enjoyed a visit with him. The traditional one carnation was attached by John Blocki, and then the celebrant was presented with thirty more carnations, one for each active member. Mr. Fuller was Honorary President A. Ph. A. 1918–1919; he was born in Connecticut in 1829; he joined the Association in 1869. The recording secretary, Fra. Wilhelm Bodemann, placed in the hands of Mr. Fuller the round robin signed by all the members at the round table.

Elmer H. Wirth, for a number of years with Frederick F. Ingram Co., is now instructor of Pharmacognosy at the University of Illinois School of Pharmacy, associated with Prof. E. N. Gathercoal.

Clyde L. Eddy, managing editor of the *Druggists' Circular*, has been elected a vice-president of the American Medical Editors' Association. This is the first time that a pharmaceutical editor has been so honored by this body.

Robert Alexander Gayle, son of **J. W. Gayle,** secretary of Kentucky Board of Pharmacy, was married November 23rd, to Miss Frances Garnett. Mr. Gayle graduated from Louisville College of Pharmacy in 1921, and was the valedictorian of his class.

C. Herbert Packard has resigned as president of the Massachusetts College of Pharmacy; he will continue to be a member of the board of trustees. Mr. Packard was elected president of the college in 1909, and is now succeeded by William H. Glover, who has been vice-president of the institution for many years.

L. E. Warren addressed the American Association of Dairy, Food and Drug Officials at its 26th annual convention, October 3rd, in Kansas City. The subject of his address was "The Laboratory of the American Medical Association and Its Work;" results of the analyses of numerous proprietary and "patent medicines" were shown by means of lantern slides.

W. Bruce Philip, vice-president of the N. A. R. D. and a vice-chairman of the House of Delegates A. Ph. A., was given a testimonial dinner by San Francisco and Alameda Associations of Retail Druggists. While the occasion was prompted by his election, it was expressive of the appreciation of California druggists for his efforts in their behalf. All interests of the drug trade were represented at the table. Mr. Philip, in writing to the JOURNAL, states: "This makes me feel that we are getting somewhere."

E. H. Gane, after twenty-five years of service with McKesson & Robbins, has severed his connection with latter firm, and has opened up an office at 1063 Sterling Place, Brooklyn, as pharmaceutical and analytical chemist.

L. A. Jeancon, general manager of Scholtz Mutual Drug Co., reports the successful opening of the San Francisco store, and preparations are well advanced for the Los Angeles establishment.

Otto Raubenheimer is now grandfather; a card under date of October 7th announces Shirley Meta, daughter of Mr. and Mrs. Herbert Raubenheimer.

E. M. Holmes, honorary member of the American Pharmaceutical Association since 1899, to whose serious accidental injury mention was made several times during the year, is now fully recovered from the effects of the accident.

Sir W. S. Glyn-Jones, honorary member of the American Pharmaceutical Association, has been elected president of the National Association of Insurance Companies for England and Wales for the ensuing year.

In the July issue of the *Journal* reference was made to the award of the Hanbury Medal for 1922 to Prof. Emile Perrot. The formal

award was made at the opening of the British Pharmaceutical Society's School of Pharmacy, October 4th. The inaugural sessional address of the reopening of the school was made by the Vice-Chancellor of the University of London, H. J. Waring. An address was also made by Professor Perrot.

The Chemist and Druggist of October 15, 1872, refers to an anecdote about Apothecary Karl Wilhelm Scheele. During his lifetime the King of Sweden, his sovereign, visited Paris, and Lavoisier and all the learned men inquired about Scheele, but his Majesty had never heard of him. He wrote home at once and ordered his ministers to look him up. The only Scheele who could be found was a clerk in one of the Government offices, so he was knighted and pensioned. But when the King returned the real Scheele was found and offered every inducement to take up his residence in Stockholm, but he preferred his shop in Köping.

The Pharmaceutical Journal and Pharmacist of October 21st reviews the YEAR BOOK of the American Pharmaceutical Association for 1920. After referring to the text matter with considerable detail the following concluding remarks are made:

"The abstracts are drawn from the literature all over the world. The subjects have been chosen with great judgment, and the volume as a whole is one which is truly representative of the best that is being done in the pharmaceutical world and eminently designed to keep the pharmacist *au courant* with the technical affairs of his calling. While a perusal of the pages of this YEAR BOOK serves to give one a good idea of the multiplicity of subjects dealt with, a glance at the general index imparts a better idea—there are twenty-six two-column pages of it and there is also an index of authors."

David Hooper writes to Secretary William B. Day—"I have to thank you for Volume 9 of the YEAR BOOK of the A. Ph. A. It is a splendid production and is of great interest."

The Carolina Journal of Pharmacy, published monthly by the North Carolina Pharmaceutical Association, is also the official organ of the South Carolina Pharmaceutical Association. The text matter is chiefly devoted to matters of immediate interest to these two state bodies. The October number contains an historical account of the famous old Charleston drug shop, now 142 years old. The article was written by Mr. John Bennett, of Charleston, and presented as a contribution to the Section on Historical Pharmacy of the American Pharmaceutical Association, Cleveland meeting.

The 70th anniversary of the founding of Meyer Brothers Drug Company of St. Louis was celebrated September 12th. The banquet was part of the program of the ceremonies, at which time men prominent in the affairs of St. Louis were speakers, and also a number of those who had for many years participated in the activities of this company, and more particularly those who gave their energetic support since February 1915, when the company passed into the hands of a receiver, and now has wiped out this indebtedness.

1867 CLUB.

At the Nashville Convention of the A. Ph. A., Otto Raubenheimer and J. Leon Lascoff, both born in 1867, conceived the idea to get together the pharmacists born that year and form a social club. For over 20 years the former has collected dates of birth and death and other happenings in pharmacy which served as a foundation for his many historical papers.

Thus the 1867 Club came into existence. An annual gathering is held in connection with a dinner, which this year took place on the evening of November 2, at the Hotel Pennsylvania, New York City. The following members were present: Dr. Alfred R. L. Dohme from Baltimore, Congressman Herman A. Metz, J. Leon Lascoff, R. E. Dyer, S. Watkins, M. Schlesinger and Wm. Roschen of N. Y. City, Otto Raubenheimer and Robert S. Lehman of Brooklyn, and C. A. Buchbinder of Winfield, N. Y. Warren L. Bradt of Albany, Francis B. Hays of North Carolina, John F. Behrens of Orange, Adolf Schmidt of Hoboken, and Emil Weiss and George S. Schweinfurth sent letters of regret for their absence. Hugo Kantrowitz of the New York *Apotheker Zeitung* was the guest of the dinner.

A delightful evening was spent and the members exchanged some of their reminiscences. The gathering did not break up until midnight, when the members present accompanied Dr. Dohme to the train for Baltimore.

Pharmacists and all those connected with pharmacy born in 1867 are eligible for admission. There are no dues or fees. Simply send your name, address and date of birth to the president, J. Leon Lascoff, Lexington Avenue and 83rd Street, N. Y. City, or to the secretary, Robert S. Lehman, 3rd Ave. & 27th St., N. Y. City, or to the historian, Otto Raubenheimer, 1341 Fulton St., Brooklyn, N. Y.

SOCIETIES AND COLLEGES.

A. PH. A. HEADQUARTERS.

"When an association purchases a home, it does more than buy a piece of real estate—it shows faith in the association's future." Some have not contributed to the American Pharmaceutical Association Headquarters Building Fund. The last report is made in the October number of the JOURNAL, p. 872. Dr. J. H. Beal, 801 West Nevada Street, Urbana, Ill., is the chairman; write him for blanks. You will contribute—why not do so now?

PHARMACY AND PUBLIC HEALTH JOINED FOR STATE EXHIBITION.

The Oregon Health Exposition was held in the Auditorium of Portland from October 26 to November 4. A feature of the exposition was a booth acquainting the public with the professional side of pharmacy and its relation to public health. The booth was under the joint management of the Oregon State Pharmaceutical Association and the Portland Retail Druggists' Association.

MAINE PHARMACEUTICAL ASSOCIATION.

Maine Pharmaceutical Association convened at Bar Harbor September 13–15. The attendance exceeded 300, quite a few members of the Massachusetts State Pharmaceutical Association were present. E. W. Moore, of Bingham, Me., was elected president and Dr. M. L. Porter, of Danforth, is secretary for the twenty-seventh consecutive year. Other officers are: *Vice-Presidents*, H. R. Alden, Lewiston; W. T. Quinn, Hallowell; J. H. DeOrsay, Waterville; *Treasurer*, Frank W. Buckman, Skowhegan. Augusta was chosen for next place of meeting.

WASHINGTON STATE PHARMACEUTICAL ASSOCIATION MEETING.

The tri-state meeting proposed by Oregon State Pharmaceutical Association, in which it was hoped to have Oregon, Washington and Idaho meet together at Pendleton in September 1923, was not approved by the Washington Association. Bellingham was selected for the next place of the state meeting. The following were elected as officers for the ensuing year: G. Elmer Brown, Spokane, *president;* R. L. Price, Hillyard, *secretary;* W. E. Hoxsey, Spokane, *treasurer*. District governors elected at last year's convention were reëlected. These are: R. L. Hunt, Everett; E. E. McMillan, Tacoma; A. D. Sloan, Yakima; F. R. Robertson, Spokane; Dr. P. H. Dirstine, Pullman; C. B. Kinne, Seattle.

PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE PURCHASES A SITE FOR NEW BUILDINGS.

The plan of the Philadelphia College of Pharmacy and Science to enlarge its accommodations by the erection of new buildings in West Philadelphia has been unanimously approved by the Board of Trustees, and property facing Clark Park, at 43d Street and Woodland Avenue, has been secured. This property is near the University of Pennsylvania.

FREE PUBLIC SCIENCE LECTURES.

The Free Weekly Public Lectures by members of the Faculty were begun October 11. The subjects announced are:

"Chemistry as an Aid in the Detection of Crime," Dr. Henry Leffmann.

"Corn and Its Products," Prof. Freeman P. Stroup.

"The Story of Glass," Prof. J. W. Sturmer.

"Vitamines," Prof. David Wilbur Horn.

"Bacterial Preparations in Common Use," Prof. Louis Gershenfeld.

"The Aluminum Age," Prof. Ralph R. Foran.

"The Making of Medicines," Prof. E. Fullerton Cook.

"The Cost of Patent Medicine," Dr. Horatio C. Wood.

"The New Alloys of Iron and Their Uses," Prof. Frank X. Moerk.

"Another Drop of Blood," Prof. Ivor Griffith.

"The Romance of Spices," Prof. Charles H. LaWall.

"Catalysis and Catalysts," Prof. Samuel P. Sadtler.

"Animal Eating Plants," Prof. Heber W. Youngken.

"Explosives and Explosions," Dr. Henry Leffmann.

At the close of the series the lectures of this year will be published in book form.

THE CHEMICAL FOUNDATION ANSWER FILED.

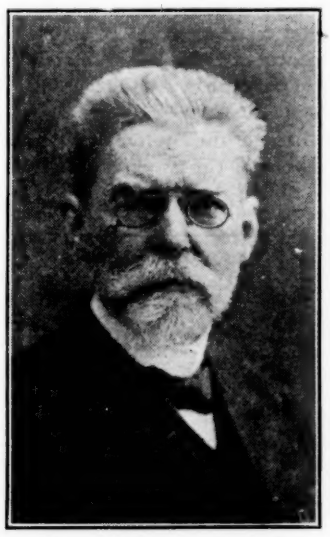
The Chemical Foundation filed its answer to the suit of the Government in Wilmington, Del., October 27. Counsel William D. Guthrie has issued a statement in which he states that the answer is a comprehensive and emphatic denial of the Government's charges.

OBITUARY.

HERMANN SCHELENZ.

Born April 9, 1848—Died September 28, 1922.

In the death of our honorary member, Dr. Hermann Schelenz, there passed away the last of the celebrated trio of pharmaceutical historians in Germany, namely, Julius Berendes of Goslar, Hermann Peters of Nurnberg and Hannover, and Hermann Schelenz of Cassel. The last named was born during stormy times when the revolution of '48 shook different parts of Europe and he died during stormy times when the "Vaterland" was trying hard to readjust itself after its defeat and downfall of the Empire. He died at Cassel, where, strange to say, Napoleon III spent his captivity after the surrender of Sedan and which city to-day is occupied by French—in fact, African troops. Indeed a sorrowful fate!



HERMANN SCHELENZ.

An extensive biography of Schelenz was prepared by the referee and published in JOURNAL A. PH. A., Vol. I, pp. 1317 and 1318, 1912, in connection with his election as honorary member at the Denver Convention in 1912. To this I might add that he has been active literary up to the very last, the *Pharm. Zentralhalle* publishing a book review from his pen in its issue of September 28, p. 515, the day of his death. Other important additions to above biography are his election as *Doctor Medicinae, honoris causa*, by the Medical Faculty of the University of Freiburg in July 1920, the offer of a chair for History of Medicine by the University of Königsberg in September 1920, and his election to honorary membership in the Deutsche Pharmazeutische Gesellschaft in February 1921.

The last book which Schelenz wrote was "Shakespeare und Sein Wissen auf den Gebieten der Arznei und Volkskunde" (Shakespeare and His Knowledge in the Realm of Medicine, etc.), published by Leopold Voss, Leipzig and Hamburg, in 1914. This first part of his Shakespeare studies was to be followed by others, but the necessary funds for publication could not be secured.

Schelenz was thankful for his election as honorary member of the A. Ph. A., as can be seen from his letter of acknowledgment in Vol. I, p. 1448. Receiving the JOURNAL regularly he abstracted many articles and published them in different pharmaceutical and chemical journals in Germany and Austria, always giving due credit to the JOURNAL OF THE A. PH. A. At the New Orleans Convention in 1921 he contributed a paper, "History of Emulsions,"* to the Section on Historical Pharmacy. In one of his last letters to the referee he expressed his sorrow that owing to circumstances and the low valuta he was unable to contribute to the subscription of the A. Ph. A. Headquarters Building Fund.

Hermann Schelenz has passed away, but his name will continue to live in the history of pharmacy as the author of that master work of nearly a thousand pages, the compilation of which occupied ten years of his life, "Geschichte der Pharmazie," published by Julius Springer, Berlin, 1904. The book will remain his everlasting monument, better than granite or bronze.

"Requiescat in Pace."

OTTO RAUBENHEIMER, PH.M.

* To be published, is now being translated.

ARTHUR MEYER.

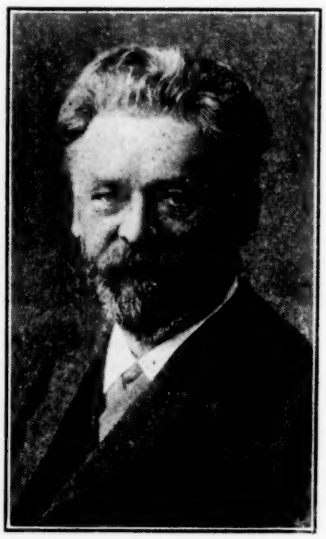
Marburg, a university town, nestles among the hills on the Lahn, a little stream which winds its way through the valleys of Hessen on its way to the Rhine.

It was at this university that Bunsen did much of his epoch-making work as a chemist. It was here, shortly before I became a student in 1895, that Behring worked out the successful manufacture of diphtheria antitoxin. There is not a faculty in the university that has not on it some scholar of distinction. When Owen Wister a few years ago referred to some half-dozen scholars of the world, Professor Cohen, of the department of philosophy of the University of Marburg, was one of them.

In pharmacy Marburg has produced two shining lights, both of whom are recognized by the American Pharmaceutical Association and were elected honorary members. Professor Schmidt, the eminent pharmaceutical chemist, attracted students from all over the world and it was from his laboratories here that he directed the researches on the plant alkaloids which have enriched our science and made master technicians. Professor Schmidt was a man of great force and power and possessed oratorical powers of a very high order. His death at an advanced age was reported in JOURNAL A. PH. A. some time ago.*

We now learn that another one of the Nestors of pharmacy in this great university has accepted the call Beyond. He was one of the two great pharmacognosists furnished by this university.

We cannot think of Marburg without recalling the work of Professor Geheimrath Wigand whose contributions to pharmacognosy were made two or more decades ago. His successor, Professor Dr. Arthur Meyer, followed in the footsteps of his predecessor and attained fame in the branches of botany and pharmacognosy. He was a worthy successor to Prof. Wigand and his contributions to science are even more voluminous. His demise will be received with regrets by his many students and by all who are familiar with his forceful writings.



ARTHUR MEYER.

Professor Meyer was an indefatigable student, and a splendid teacher. It was in the spring semester that he gave his lectures in botany and these were held at 7 o'clock in the morning. The auditorium was packed to capacity and his lectures were enjoyed by all classes of students. Like other German professors, he took nothing for granted and his lecture table was always filled with living specimens and apparatus. The walls were lined with charts. On the floor were large plants in tubs and it is no exaggeration to say that every foot of available space was utilized.

One of the most remarkable demonstrations which I ever saw was his mechanical device illustrating the mechanism of the stoma. It was worked out most carefully according to the laws elaborated by Schwendener. Into the guard cells was forced air simulating the water supplied by the plant and as they became inflated or turgid the pore became visible just as in the growing plant. He had every mechanical device and indeed conducted the whole line of experiments to elucidate the subjects of his lectures.

Professor Meyer when not at lectures was in his laboratory. He was always at work on some morphological problem. He, however, never lost his interest in his pharmaceutical studies. He had served as an apprentice in pharmacy in Nordhausen and he seems always to have felt an obligation to do something for the profession which adopted him and which he used as a stepping stone for his scientific career. His two volumes on "Scientific Drug Knowledge" are one of the greatest contributions ever made to pharmacognosy. He wrote many other scientific papers on drug subjects and never lost an opportunity to bring the importance of pharmacognosy

* December 1921, p. 965.

to the attention of others. His article advocating the appointment of professors in pharmacognosy in German high schools shows how much at heart he had his subject.

Professor Meyer had a keen insight into the ultimate structure of living organisms. He was a master in subjecting his observations to very careful scrutiny. Like DeBarry, his great teacher, he made few if any mistakes and when there was any doubt his language revealed his own uncertainty. It is difficult to say which of his works will endure the test of time. His earlier work on the starch grain was probably equal to Nageli's master work on the same subject and which was considered by Wallace to be one of the greatest intellectual feats of the last century.

Professor Meyer's studies on bacteria are by no means a small contribution to this science. His Handbook without doubt is one of the best books which has been written. When he took up any study he always penetrated further than his predecessors. He illuminated the subject and always saw inside of the living cell. If there were living organisms like bacteria, he was not content, like the average worker in bacteriology, to see what they did when planted on culture tubes, but he observed them as they were swimming about and the result of this work was to show that bacteria by means of their movements could be distinguished and even classified.

Professor Meyer liked to write books. He was not satisfied with a few papers as we call them, but he rounded out the subject, and so we find that his "Handbook of Botany," dealing with the microscopical study of plants, has been very much appreciated by laboratory workers. It far excels a similar work by Strasburger which was a popular work and an English translation was used by students in this country.

Professor Meyer loved his students and was beloved by them. He was always ready to criticize their work and there was a warmth in his voice and a twinkle in his eye for the earnest student. To the ambitious he was an inspiration to achieve the highest results. He was a great disciplinarian but his discipline was prompted by love for his students and his devotion to science. He was above all things most persevering in the pursuit of facts. He cultivated the habit of active attention and inculcated in his students those habits of attention which make masters. Professor Meyer possessed a fine character and was very fortunate in having as a helpmate a wife who appreciated his work and at the same time saw to it that he had the needed relaxation. I have often seen her come to the laboratory during the day to bring him some message. She was a very careful housekeeper and their entertainment of friends was very delightful. They liked to stroll in the neighboring forests and both were very fond of outdoor life. Under these circumstances work, even the hardest, is full of pleasure and leads to the Elysian fields. Professor Meyer's life is indeed an inspiration; starting as a drug clerk he studied under the masters of science and himself became a master and a guide, blessing all those who came under his benign influence.

HENRY KRAEMER.

MRS. LEWIS C. HOPP.

We have been advised of the death, on November 2, of the wife of Lewis C. Hopp, president of the American Pharmaceutical Association, 1903–1904. All members of the Association will sympathize and sorrow with Mr. Hopp and his daughters in the bereavement. Mrs. Hopp and one or the other or both of the daughters usually accompanied Mr. Hopp to the annual conventions of the A. Ph. A.—he never came alone.

At Cleveland, the family shared in the success of that meeting; Mrs. Hopp always contributed to the happiness of the annual occasions, entering into the entertainments with that same interest shown by her in contributing to the success of these features in Cleveland. She also presided over the Women's Section A. Ph. A., 1920–1922.

DR. ALBERT O. ZWICK.

Dr. Albert O. Zwick, the first president of the Ohio Valley Druggists' Association, and one of the active members of the National Association of Retail Druggists and for a number of years of the A. Ph. A., died at his home in Cincinnati October 21, aged 56 years. He was one of the incorporators of the American Druggists' Fire Insurance Company, and a director. The deceased is survived by his wife and one son, an interne in Speers Hospital, Dayton, Ky.

BOOK NOTICES AND REVIEWS.

REVIEW OF THE FOURTH EDITION OF THE PHARMACOPOEIA OF JAPAN—ENGLISH TRANSLATION.

BY A. G. DUMEZ.

The Fourth Revised Edition of the Pharmacopoeia of Japan was completed in May 1920 and appeared in print the following year. It represents the results of the labors of a committee of 21 members, a chairman, and a secretary, appointed by the Minister of Home Affairs. The actual work of revision covered a period of 5 years and 2 months, having been begun in March 1915. In this revision 73 new items were added, 94 items were deleted and 1400 alterations made, besides numerous changes in the terms and wording of the monographs.

The English translation of this Edition is the work of the Publication Committee of the Pharmaceutical Society of Japan. It was completed in March 1922, just 1 year and 10 months after the Committee of Revision finished its labors. This is indeed a remarkable feat, and the members of the Publication Committee having this work in charge are to be commended for the rapidity with which they worked and the high degree of excellence attained. While the English is awkward in places, the meaning is clear in all cases and the usefulness of the volume is in no-wise diminished thereby.

The new volume contains a total of 534 pages, 28 of which are devoted to introductory and explanatory notes; 437 to drugs, chemicals and preparations; 20 to reagents and volumetric solutions; 19 to tables; and 30 to the index. The form of arrangement and sequence is very similar to that of the Ninth Revision of the Pharmacopoeia of the United States.

The introductory matter includes, in addition to the historical introduction and preface, a chapter headed "Introductory Notes." This chapter contains details of a specific nature such as a statement defining the arrangement of the material in the monographs; definitions for such terms as *tepid, warm, hot, hot extraction, cold extraction, parts by weight, weighable, et cetera,* also definitions for the degree of fineness of comminuted drugs; and directions for determining rotatory power, melting points, congealing points, boiling points, acid values, saponification values, ester values and iodine values.

The main portion, or body, of the book contains the monographs on the official articles. In this portion there are 688 titles arranged alphabetically. Nineteen of these titles are class headings, *viz.:* **Capsulae, Decocta, Elaeosacchara, Electuria, Emplastra, Emulsiones, Extracta, Extracta Fluida, Infusa, Linimenta, Pastae, Pastilli, Pilulae, Pulveres, Saturationes, Sirupi, Species, Spirituosa,** and **Suppositoria.** Under each of these headings, there are given specifications for standards to which the articles of the class should conform or general directions for methods of preparation. The new titles of which there are 73 are: **Acetonum, Acidum diaethylbarbituricum, Aethylium chloratum, Aethylmorphinum hydrochloricum, Agar-Agar, Antipyrino-Caffeinum citricum, Argentum colloidale, Benzaldehydum, Benzolum, Bismutum jodatum subgallicum, Calcium chloratum, Calcium lacticum, Capsulae, Chloroformium pro narcosi, Cortex Cinnamomi Loureirii, Emetinum hydrochloricum, Emplastrum saponatum salicylatum, Emulsiones, Emulsio Olei Jecoris, Electuaria, Ferrum sulfuricum siccum, Folia Scopoliae, Herba Swertiae, Hydrargyrum sulfuratum rubrum, Kalium sulfoguajacolicum, Lignum Santali album, Limonada citrica, Limonada hydrochlorica, Linimenta, Liquor Aluminii acetici, Liquor Gelatinae sterilisatus, Liquor Hydrogenii peroxydati, Liquor Jodi compositus, Liquor Kali caustici, Liquor Natrii chlorati physiologica, Liquor Ringeri, Methylenum coeruleum, Natrium thiosulfuricum, Oleum Arachidis, Oleum Pruni armeniacae, Oleum Tsubaki, Paraaminobenzoyldiaethylaminoaethanolum hydrochloricum, Pastae, Pasta Sulfuric cum Pice liquida, Pastilli Acidi acetylsalicylici, Pastilli Chinini hydrochlorici, Pastilli Kalii jodati, Pastilli stomachici, Phenolphthaleinum, Pilulae Acidi arsenicosi, Pilulae Ferri et Chinini, Pilulae Guajacoli carbonici, Pilulae Kreosoti carbonici, Pulveres, Pulvis stomachicus, Pulvis Qinci cum Amylo, Pyoktaninum ceoruleum, Radix Polygalae, Saturationes, Sirupus Abelmoschi, Sirupus Polygalae, Spirituosa medicata, Talcum depuratum, Theophyllinum, Tinctura Jodi diluta, Todaiwo, Tropacocainum hydrochloricum, Unguentum Argenti colloidalis, Unguentum basilicum, Unguentum camphoratum, Unguentum Willkinsoni, Unguentum Wilsoni, Vaselinum flavum.** The items which were official in the previous edition but which were not admitted to the new edition, numbering 94 in all, are: **Acetum aromaticum, Acetum Scillae, Acidum carbolicum crudum, Albumen Ovi siccum, Anetho-**

lum, Aqua Amygdalarum amararum, Aqua Anisi, Aqua Carvi, Aqua Picis, Arsenum jodatum, Carrageen, Carvonum, Chininum bisulfuricum, Collemplastrum, Cortex Mezerei, Extractum Aconiti Napelli, Extractum Cardui benedicti, Extractum Cascarillae, Extractum Phyostigmatis, Extractum Phytolaccae, Extractum Ratanhiae, Flores Arnicae, Flores Chamomillae romanae, Flores Malvae, Flores Rosae, Flores Sambuci, Flores Tiliae, Flores Verbasci, Folia Althaeae, Folia Belladonnae, Folia Bucco, Folia Coco, Folia Farfarae, Folia Melissae, Folia Trifolii fibrini, Fructus Carvi, Gossypium carbolisatum, Gutti, Herba Cardui benedicti, Hydrargyrum cum Creta, Kino, Lapis Pumicis, Lignum Santali rubrum, Liquor Arseni et Hydrargyri jodati, Liquor Ferri oxychlorati, Liquor Nitroglycerini, Magnesia usta ponderosa, Magnesium carbonicum ponderosum, Mel rosatum, Nitroglycerinum, Oleum Hyoscyami, Oleum Juniperi, Oleum Lauri, Oleum Myristicae aethereum, Oleum Resinae empyreumaticum, Oleum Sabinae, Oxymel, Oxymel Scillae, Paraldehydum, Pastilli Acidi borici, Pastilli Ferri lactici, Pastilli Kalii chlorici Pastilli Menthae, Pastilli Natrii bicarbonici, Pilulae Aloes et Asae foetidae, Pilulae Chinini sulfurici, Pilulae Colocynthidis et Hyoscyami, Pilulae Ferri carbonici Blaudii, Pilulae Hydrargyri, Pulvis aerophorus laxans, Radix Gelsemii, Radix Phytolaccae, Radix Ratanhiae, Radix Serpentariae, Resina Dammar, Semen Tonco, Sirupus Croci, Sirupus Sennae cum Manna, Sparteinum sulfuricum, Species laxantes, Species pectorales, Spiritus Juniperi, Tinctura Aloes, Tinctura Gelsemii, Tinctura Lavandulae composita, Tinctura Ratanhiae, Tinctura Scillae, Tinctura Serpentariae, Unguentum Paraffini, Unguentum stibiatum, Unguentum sulfuratum, Veratrinum, Vinum stibiatum.

In the selection of items to be admitted, the Committee of Revision appears to have acted most conservatively. The articles deleted are, with few exceptions, either obsolete or of little medicinal value. The articles admitted are for the most part identical with those contained in other modern pharmacopoeias, except that preference has been given to Japanese pharmaceutical chemicals and drugs. This is especially true in the case of vegetable drugs as is clearly shown by the recognition of the following as official: the leaves of *Scopolia japonica* Maxim., the leaves of *Datura tatula* L., the leaves of *Mentha arvensis* L., var. *vulgaris* Benth., the leaves of *Prunus macrophylla* Sand Z., the bark of *Cinnamomum Loureirii* Nees., the roots of *Abelmoschus manihot* Medic., the root of *Gentiana scabra*, the rhizomes of plants belonging to the genus *Coptis*, the rhizomes of *Dryopteris crassirhizoma* Nakai, the rhizome and roots of *Valeriana officinalis* L., var. *latifolia* Miq., the rhizomes of plants belonging to *Rheum* grown in Japan, the herb of *Swertia japonica* Makino, the seeds of *Prunus armeniaca* L., the tuberous roots of plants belonging to *Orchis*, *Anacamptis* or *Cremastra*, and the oil expressed from the husked seeds of *Camellia japonica* L. With respect to the newer remedies admitted, it might be said that the Committee was ultra-conservative. While such substances as aspirin, lactophenin, novocaine, orexin tannate, protargol, pyramidon, salipyrin, tannalbin, tannigen, theophyllin, thiocol, trional, veronal and xeroform are included in this list, such important remedial agents as the arsphenamines, suprarenal gland or epinephrine, pituitary, and thyroid have not been given recognition. Among the galenical and pharmaceutical preparations now obsolete or little known in this country are preparations belonging to the following classes: oil-sugars, electuaries, pastes, pastils, saturations (mixtures containing CO_2, prepared by the saturation of solutions of acids with alkali carbonates), species, medicated cottons and medicated gauzes.

To one accustomed to the nomenclature of the United States Pharmacopoeia, some of the titles seem queer, *i. e.*, **Adeps Lane cum Aqua, Aqua Carbolisata Pro Disinfectione, Calcaria Chlorata, Carbo Ossium Pulveratus, Fructus Aurantii Immaturi, Pastilli Stomachici, Pulvis Aerophoris, Pulvis Infantum, Stibio-Kalium Tartaricum, Stibium Sulfuratum Aurantiacum, Unguentum Hebrae, Unguentum Wilsoni, Unguentum Vesicans Fortius.** And, when one encounters **Paraaminobenzoyldiaethylaminoaethanolum Hydrochloricum,** it is realized that the American physician is not the only one who has trouble with pharmacopoeial nomenclature.

That portion of the book devoted to reagents and test solutions is not nearly as complete as that given in the Pharmacopoeia of the United States. While there are listed 158 reagents, the specifications given are very brief. Only 16 volumetric solutions are listed and in no case are directions for preparation given—only specifications for strength and a few equivalents are given.

The only tables appearing in the book are the following: (1) A list of the common official medicines which should always be kept in a dispensary. (2) A list of official medicines, which belong to the class of poisonous medicines, and which should be preserved with special care, separate from the others, in a cabinet or cupboard that can be closed. (3) A list of official medicines, which belong to the class of strong or powerful medicines, and which should be preserved with care, separated from the others. (4) A table of maximum adult doses. (5) A table giving the names, synonyms and atomic weights of the more important elements. (6) A comparative table of the official and popular names of the newer remedies.

Leipzig is the "book center " of the entire world. The Bibliographisches Institut (Bibliographic Institute) in Leipzig is one of the foremost publishers who specialize in high class books. The firm favored us with the following two works for review:

Die Pflanzendecke der Erde. Eine allgemeine Pflanzengeographie von Dr. Adolph Hansen. 276 pp. 1 map and 24 illustrations.

It is a credit to pharmacy that the author of this work was an apotheker, who became professor of botany at the University of Giessen where he died on June 24, 1920. Plant geography is that branch of botany which deals with the distribution of the various plants in different parts of the world and its underlying causes. After his travels in the tropics (1799–1804) Alexander von Humboldt became the father of this special field of botany, as laid down in his book, "Ideas to a Plant Geography" (Stuttgart 1807).

The first part of the book, the Introduction, deals with the flora in general, its history, development and the changes caused by the influence of man.

The second part comprises the Vegetation of the Earth, divided into the following parts: Arctic Zone, Europe, Asia, Africa, Australia and the Islands in the Pacific Ocean, America and the Antarctic Zone.

The author points out that the present plant population of the different parts of the world have arisen from various sources, undergoing different processes of development in the course of ages. Even though physical conditions be equivalent at the present time on two points of the world, the plant materials which had to change and adjust themselves to these new identical environments may have been originally different. Even in nature evolution is constantly progressing!

The referee begs to call special attention to the historical part of the book to which 10 pages are devoted, beginning with the works of Theophrastus about 305 B. C. who can be rightly called the father of botany. The history of that 15 folio volumes master work, "Flora Brasiliensis" (1840–1905), is also given in detail.

A large map in colors shows at a glance the distribution of the different forms of vegetation over the world. Six plates contain 24 excellent illustrations of plants from all parts of the world and help to illustrate the book and elucidate its contents. Thanks are due to the publishers for this part of the work.

The book is a work of art and should become better known among teachers, pharmacists and the public in the United States, quite specially as books on plant geography are not too abundant.

Weltgeschichte, 9. Band: Amerika and Australien. Lex. 464 pp.

The classic work "Helmolt's History of the World" is now complete in its second edition after 12 years of hard work. Volume 9 before us treats America and Australia together with an index for the entire set. The history of America has been written by Prof. Dr. Konrad Haeberland, and Dr. Johannes Hohlfeld, both expert historians.

How broad and thorough the subject is treated can be seen from the following chapters: Aborigines of South, Central and North America, Central American Culture, South American Culture, Discoveries and Conquests. Spanish Colonies, British Colonies, War of Independence of North America and South America, United States since 1820, Antilles, Canada, Independent South America, Central America and Brazil. Richly illustrated with 2 maps, 3 colored plates, 8 printed plates and 68 illustrations in the text, the book before us is a work of art.

It is the pride of Americans that our hemisphere has contributed its share and over, to the sum total accomplished by the entire world. For that reason it is well to learn that two outsiders, two German professors, hold that very same opinion. We can recommend this book very highly.

OTTO RAUBENHEIMER, PH.M.